

What is *Nature* for?

JOURNALS which too frequently assault their readers with introspection about their functions run several risks, the most immediate of which is that they will be boring and the most serious that they will be so enmeshed by policy statements and declarations of objectives that they find themselves having to choose between flexibility and consistency. In the nature of things, the relationship between a journal and its readers is bound to be—and should be—so much less tangible that formal definition is not merely impossible but undesirable. Journalism, after all, is a means by which a group of readers is given a sense of community by its dependence, however incomplete, on what is published issue after issue. This is the sense in which a journal belongs as much to the readers as the writers. *Nature* has been fortunate, in the past 103 years, in the strength of this sense of community. It is a constant pleasure that readers and contributors regard the journal with fondness—and those who complain do so, more often than not, in sorrow, not anger. The special quality of *Nature* stems as much from this intimacy as from the way in which it has been able to publish the first accounts of some of the distinguished research. And there is no doubt that this special intimacy between readers and contributors will continue even though there is about to be a change of editor (see page 110)—a rare event. Dr David Davies, who takes up this appointment at the end of August, will be only the fifth editor of *Nature* in more than a century (a calculation somewhat complicated by the joint editorship of Mr A. H. V. Gale and Mr L. J. F. Brimble from the Second World War until Mr Gale's retirement and Mr Brimble's later death in 1965).

Why has *Nature* succeeded so well? At the beginning, *Nature* was much more a gossip sheet than a learned journal, as can be told from the extracts from old volumes now published in each issue. It was a means of informing scientists of the late nineteenth century, without other means of communication, of events of general as well as special interest. The departure of the Challenger on its cruises, or the preparations for the next eclipse, were the raw material of *Nature* for the first several years. From the start, however, there was information about the proceedings of foreign academies, a strong and intelligent approach to the published literature of science (including not merely book reviews but reviews of scientific articles appearing in what were then called the scientific serials) and a miscellaneous range of correspondence dealing as much with natural history and natural phenomena as with the kinds of scientific subjects which now constitute a scientific letter. But from the start, *Nature* was a robust critic of the way in which science was managed. The early issues were full of complaints at the British Government's neglect of such good causes as the need to observe eclipses wherever they occur, the need to manage institutions such as the Kew Observatory intelligently and the need for public education in science. While the sense of intimacy which is the first prize of journalism no doubt sprang from the usefulness of the information which it

gathered, its public influence depended on the aptness and outspokenness of its opinions. Only towards the end of the nineteenth century was begun the tradition of communicating news of original discovery directly to *Nature*.

It is fair to claim that such success as *Nature* has since enjoyed stems from the pursuit of the old objectives, implicit though they may have been. To be sure, methods have changed with changing circumstances. The days have gone when a decision to publish or decline a scientific article could be determined in the office, by the reputation of the author or the quality of his address. Inevitably, research has become more and more a pursuit for specialists, with the result that it is hard to work to the old ideal that every reader should, if so inclined, be able to read *Nature* from cover to cover. (Even so, it is something of a surprise that fields such as molecular biology have become in the past decade almost inaccessible to all but the specialists.) The increasing competitiveness of research has also created new pitfalls—in reviewing scientific articles which have appeared elsewhere, for example, there is now a much greater risk than in the nineteenth century that an honest researcher will be deeply hurt if it seems that his own work has not been given proper credit. News and general information is easier to collect but ages more quickly. And opinions, however well-considered, are more easily lost than ever among the general noise of public comment. Yet there is no reason to think that the traditions of the past century have become inappropriate nor to fear that, with modification no doubt, they will lightly be abandoned. There is no reason why the second century should not be even more successful—and amusing—than the first.

100 Years Ago



A *résumé* of our knowledge, strikingly incomplete as it is, on the subject of sneezing, is given by Dr. Seguin in the third number of the new and excellent *Archives of Scientific and Practical Medicine*. The author's attention was drawn to the subject from his observing a fact, previously well known, that sneezing may be frequently stopped by pressing the fingers on the lips or sides of the nose. No new theory is given to explain the physiology of the phenomenon, and it is stated that naturally most of the air expired during a sneeze escapes through the nose, but that custom has brought about the discharge of a part through the mouth. This we cannot agree with, as it is difficult to believe that custom has much influence on so abrupt an act.

From *Nature*, 8, 76, May 22, 1873



OLD WORLD

Geophysicist to be Editor of *Nature*

DR DAVID DAVIES, leader of the Seismic Discrimination Group at the Lincoln Laboratory of the Massachusetts Institute of Technology, is to be the next editor of *Nature*.

Dr Davies will take up his new position at the end of August. Mr John Maddox, who has edited the journal since February 1966 is leaving *Nature* today but until Dr Davies takes up his appointment *Nature* will be edited by Dr Alun Jones the present Deputy Editor.

Dr David Davies is 33 years old and was educated at Nottingham High School and Peterhouse, University of Cambridge from where he graduated in physics in 1961. Since then he has been involved in research in geophysics; first as a graduate student at the Department of Geodesy and Geophysics at Cambridge, then as a senior assistant in research at the same department and, since January 1970, at MIT. Dr Davies was also a fellow of Peterhouse from 1946 to 1969.

Dr Davies's early research was concerned with the exploration of the ocean floor and its underlying geology by seismic methods. During this time he participated in cruises in the Atlantic Ocean, Indian Ocean, Gulf of Aden and the Red Sea. It was as a consequence of this work that Dr Davies developed an interest in providing a theoretical explanation for signals recorded as a result of explosions and his doctorate thesis was also devoted to these problems.

Since 1966 Dr Davies's interests in seismology have broadened and in 1968 he was the rapporteur to the Seismic Study Group convened by the Stockholm International Peace Research Institute.

At this meeting eleven seismologists from ten countries reconsidered the evidence bearing on the detection and identification of underground nuclear weapons tests. One of the results of this meeting is that there is now wide agreement on the scope and limitations of seismology in policing any test ban. The inadequacy of seismic monitoring had been one of the chief reasons why the Test Ban of 1963 had not included underground explosions.

During the past three years Dr Davies has been deeply involved in the remaining problems associated with the policing of a test ban treaty. In particular, he has used arrays of seismic detectors spread over areas of diameter two

hundred kilometres in Montana to determine whether nuclear explosions can be distinguished from earthquakes. As well as what Dr Davies calls this "mission oriented research" the arrays have been used to determine the nature of the Earth's core and to determine how seismology can be used in plate tectonics. Recently the existence of lateral heterogeneity deep in the Earth

has also been detected by such large arrays.

In 1966 Dr Davies edited a special volume of the *Geophysical Journal* of the Royal Astronomical Society and soon afterwards he became an editor of that journal. He is now one of its two North American editors. Dr Davies has also been *Nature's* geophysics correspondent since 1968.

PHARMACEUTICALS

Drug Research

LARGE pharmaceutical companies tend to produce more results from their research and development than small ones. This conclusion, in direct contradiction to that reached by the Monopolies Commission, was presented recently at a conference on innovative activity in the pharmaceutical industry organized by the National Economic Development Office. Mr George Teeling-Smith, Director of the Centre for the Study of Industrial Innovation, presented data from a report that is due to be published shortly by the CSII, which shows that there is a linear relationship between the output of new products and research and development expenditure. This contrasts with the non-linear relationship found by the Monopolies Commission.

The difference between the two conclusions is probably explained by the fact that CSII did not use the conventional measure of pharmaceutical companies' research success—the number of patents each company files. Conclusions based on patent filings could be dangerously misleading, Mr Teeling-Smith said, because, for example, companies file patents at different stages in the development of drugs.

Instead of counting patent filings, Mr Alan Angille, who carried out the work for CSII, attempted to identify all the new pharmaceutical compounds introduced to world markets between 1958 and 1970. Inevitably coverage was incomplete for compounds originating in, for example, Japan, but it clearly showed that the laboratories producing the largest number of innovations also produced those that were the most successful.

Mr Angille then studied in detail twenty companies who could provide an account of their new products and their research expenditure over a period of one year. The firms chosen represent

"a good spread across the spectrum of expenditures in the industry", according to Mr Teeling-Smith, and the study showed that the larger companies tended to be the more productive.

Clearly much larger studies need to be carried out, but CSII's work does suggest that the "conventional wisdom" which led the Monopolies Commission to oppose the Beecham, Boots, Glaxo merger should "be put into cold storage until further soundly-based studies can throw further light on the whole subject", according to Mr Teeling-Smith.

The Monopolies Commission was also criticized by Mr R. D. Douglas, Director and Legal Adviser to Pfizer Ltd, who suggested that because "winners" in the pharmaceutical industry are so elusive and unpredictable, companies rarely enjoy really high profits. Those made by Hoffman-La Roche, which the government is currently criticizing, were calculated by the commission in a "surprisingly crude way", Mr Douglas said. Of greater danger, he said, were the new breed of pharmaceutical companies which marketed at cut prices drugs that others had developed and patented. These companies succeed because actions over patent infringements take so long to complete. One such action, started in 1963, was not concluded until last year.

The time scales involved in drug development are lengthening, and this also worried delegates to the conference. The delay between the initial screening of a compound and its launch is growing, as is the time it takes to reach peak sales.

Equally the time the Medicines Licensing Authority takes to grant permission for clinical trials was criticized by Dr D. G. Davey, Director of Research at ICI, although Dr F. Hartley and Professor O. L. Wade, two members of the commission, suggested that the remedy lies at least partly with the industry. Good submissions can be processed more quickly, they said.

ENVIRONMENT

Charting Chemicals

from a Correspondent

AN information network on chemical substances and their effects on the environment would be valuable, according to the Royal Society's British National Committee for Problems of the Environment. This was the outcome of a meeting held recently in London under the auspices of the committee and attended by 200 participants, which included representatives from the European Economic Commission, the OECD, and the United Nations Environment Programme.

The purpose of the meeting was to discuss the feasibility and usefulness of collecting into a centralized network existing data on known chemicals in order to predict any possible future adverse effect from chemicals with broadly similar properties. In the wider context these data could provide a guide to environmental management policies.

The meeting also called for a reconciliation of the voluntary methods used in Britain for controlling substances introduced into the environment with the legally enforced methods used by most other countries within the EEC.

It was pointed out at the meeting that there was very little known about ecological toxicity compared with the great deal of information available on human toxicology. A call was also made for the participants at the meeting to provide specimen input on relevant environmental sources so that a demonstration project could be mounted in time for the first session of the governing council of the United Nations Environment Programme which is to be held next month.

The conclusions of the meeting, which was organized by Sir James Cook and Sir Frederick Warner, will be discussed by the British National Committee with a view to the committee formulating recommendations which might be put to the government at some time in the future.

SPACE

Belgians Protest

THE European Launcher Development Organization may yet refuse to die quietly. When the French and Germans announced at ELDO's last council meeting on April 27 that they were withdrawing financial support from the Europa II launcher project as of May 1, the chief reaction was silence. Even the British press, which might have been expected to announce that Britain had been right to pull out of the organization in 1968, largely ignored the event. It looked as though the organization could be killed far more easily than many had thought possible.

But Belgium, which only found out about the Franco-German decision in the council chamber, has decided, after thinking about it for a fortnight, to register its protest, and the staff of ELDO has issued a statement explaining exactly what it thinks of the organization's history.

In a statement issued last week, Mr Charles Hanin, the Belgian Science Policy Minister, and chairman of the European Space Conference announced that he intended to convene a meeting of the conference shortly, and made it clear that he is far from happy with the attitude of the French and German governments. Belgium too had a substantial interest in Europa II, Mr Hanin said, but its government was never consulted. It is clear that when the conference does meet—probably in early July—a few explanations are going to be needed.

The ELDO staff in its statement condemns the attitude of the member states, and points out that the Europa project was killed before the organization's new structure—devised after the failure of F11 in November 1971—had had a chance. The staff "refuses to be associated with the responsibility for the waste of not completing a programme of such heavy capital investment, of which very little use can be made even if the L3S programme is carried out.

"It is clear that the failure of these programmes is primarily due to the political incapacity of the member states to define a common purpose and work together in a genuinely cooperative spirit," the staff says. The next launch had been scheduled for October 1, 1973, and the ELDO staff "protests strongly at the political failure of the member states being presented to public opinion as a technical failure discrediting their professional ability".

But while the ELDO staff and the Belgium government may be justifiably angry at the speed with which they were presented with a *fait accompli*, the Belgians are still eager to continue work on L3S, the launcher proposed by France. Mr Hanin, however, made it clear that he would be happier if the launched is managed by a European organization rather than by France.

ELDO, however, is most unlikely to manage the programme, even though the organization as such still exists, and may continue to do so until the new space agency comes into existence (see page 126). The Belgians will propose, however, that ELDO should organize the collection of the European money that will be put into the L3S programme if it goes ahead. But it has been suggested that the launcher might even be managed by the European Space Research Organization as a special project in the same way that ESRO manages the Spacelab programme.

SCIENCE RESEARCH COUNCIL

New Chairman

PROFESSOR S. F. EDWARDS was named last week to succeed Sir Brian Flowers as chairman of the Science Research Council in October. Professor Edwards, who is 45, is currently John Humphrey Plummer Professor of Physics at the University of Cambridge.

Professor Edwards will take full time leave of absence from Cambridge during his tenure as chairman of the SRC, which, in the first instance, will be for four years. He has also taken up an existing vacancy on the council until the time he becomes chairman.



Professor S. F. Edwards

Professor Edwards was educated at Bishop Gore Grammar School, Swansea, Gonville and Caius College, University of Cambridge, and Harvard. He also spent a year at the Institute of Advanced Study at Princeton in 1952 before taking up a post at the University of Birmingham. He moved to Manchester in 1958 and became professor of theoretical physics there in 1963. He has been a Fellow of the Royal Society since 1966 and a vice-president of the Institute of Physics since 1970. He has served the SRC in various capacities since 1968.

The retiring chairman and the new chairman of the council have had remarkably similar careers. Both were educated at Bishop Gore Grammar School in Swansea and at Gonville and Caius College at Cambridge. Both are theoretical physicists but with quite different interests — Sir Brian is a nuclear physicist whereas Professor Edwards' chief interests lie in chemical physics. Both have also held chairs at the University of Manchester and been on the staff of the University of Birmingham.

NEW WORLD

No Treaty Without Inspection

by our Washington Correspondent

SPOKESMEN for the Nixon Administration last week took an uncompromising stand on the need to include provisions for on-site inspection in any treaty banning underground testing of nuclear weapons. Their statements, made to the Senate Subcommittee on Arms Control, indicate that the Administration is not yet prepared to propose new initiatives to break the ten-year impasse in negotiations for a comprehensive test ban treaty.

But a number of other witnesses, including scientists, senators and the man who negotiated the partial test ban treaty in 1963, argued that the time is now ripe for an agreement banning all nuclear testing, and urged President Richard Nixon to pave the way for a formal treaty by seeking agreement with the Soviet Union for a mutual moratorium on underground tests. The forthcoming summit meeting between Mr Nixon and Mr L. Brezhnev, which will probably take place next month, would be an ideal time to announce such a moratorium, they suggested.

The focus of the hearings was a resolution introduced into the Senate earlier this year by Senator Edward M. Kennedy, and now sponsored by some thirty-three of his colleagues, which calls for a moratorium on underground testing and for President Nixon to offer fresh proposals for a comprehensive test ban (see *Nature*, 241, 361; 1973). But Administration witnesses opposed the resolution last week because they believe that a treaty banning underground tests could not be adequately policed unless it contains a provision for on-site inspection to determine whether possible violations have taken place. That has always been the chief stumbling block in the path of negotiations for a comprehensive test ban treaty, for while the United States has been unrelenting in its insistence on on-site inspection, the USSR has been just as insistent that national means of detecting explosions—seismometers, surveillance satellites and other intelligence—would be sufficient to guard against violators.

In some respects, Administration witnesses last week took a firmer line on on-site inspection than they did during the last round of Congressional hearings on the test ban in 1971. Their argument is that in spite of significant progress during the past ten years, seismological techniques are not able to detect all low yield explosions and, perhaps

more important, there are a number of seismic events each year which cannot be identified definitely as either explosions or earthquakes on the basis of their seismic signals.

Dr Jack Evernden, a seismologist with the Arms Control and Disarmament Agency, told the subcommittee that there would be "10 or so" events a year in the USSR with a magnitude of 4.0 or more on the Richter scale (equivalent to an explosion of one or two kilotons fired in solid rock) which could not be positively identified by national means. On-site inspection would be needed to determine the nature of such events, the Administration witnesses suggested, and Dr John S. Foster jun., Director of Defense Research and Engineering, flatly stated "with the inadequacies inherent in the seismic verification techniques, and which are likely to persist in any future system, it is necessary to supplement this technique with other verification modalities".

But that position was contested by several witnesses. In particular, Dr Herbert Scoville, former Deputy Director of the CIA, pointed out that very small events—below about 0.5 kilotons—would not be detected at all because their signals would be lost in the background seismic noise, and in those instances there would be no reason to inspect. He also said that the anomalous events which cannot be positively identified lie in a small range—between 0.5 and one or two kilotons—and a possible evader could not be certain that any specific test would remain unidentified. "It is clear," he said, "that on-site inspections serve almost no useful purpose in verifying a comprehensive test ban."

Dr Scoville and Dr Wolfgang K. H. Panofsky, Director of the Stanford Linear Accelerator, also pointed out that the US dropped its insistence on on-site inspection in a similar set of negotiations—those which led to the signing of

AUTO EMISSIONS

Detroit Concedes

by our Washington Correspondent

THE prospect of a long fight between the automobile manufacturers and the Environmental Protection Agency over emission standards receded this week, when the four largest motor manufacturers announced that they will comply with the interim standards for 1975 vehicles, introduced as a compromise on April 11. The interim standards, less severe than those originally proposed, require that carbon monoxide and hydrocarbon emissions should be reduced by 83 per cent in the United States as a whole, and by 90 per cent in California. What the manufacturers now say is that the California requirements in themselves entail the use of catalytic convertors in the exhaust systems of new automobiles, and that they may just as well be ready to install the devices on cars intended for some other parts of the United States as well. Although it would have been possible to appeal against the imposition of the interim standards, the manufacturers said last week that they could not afford to risk the substantial

delay that would have followed.

Argument about emission standards and their consequences is likely, however, to continue. Last week, the Federation of American Scientists put out, in its newsletter, a complaint against the use of catalytic convertors for reducing the amounts of pollution in auto emissions, especially now that the Environmental Protection Agency is preparing to set less ambitious goals for the emission of nitrogen oxides. The FAS statement echoes the commendation of the stratified charge engine put out last year by the National Academy of Science and asks that consumers should be protected from the risks that catalytic convertors will fail, sometimes without car owners knowing what has happened. The FAS is also concerned that the catalytic convertors entail greater fuel consumption, and asks not merely that consumers should be given objective information about the fuel consumption of new motor cars but also that the EPA should re-examine its policy on auto emissions so as to take account of the consequences for the fuel economy. It estimates that the use of catalytic convertors may entail an extra cost of \$270 a year for each car.

the SALT agreement on ABM systems—and Mr Averell Harriman, former US Ambassador to the USSR and chief negotiator for the partial test ban treaty a decade ago, added that he believes the USSR would not sign an agreement which it intends to violate.

Those who argued in favour of the senate resolution suggested that the advantages of stopping nuclear tests would be outweighed by the disadvantages that may result from possible violations. One key question in such a determination is the military significance of small nuclear tests, and that, of course is classified. But Dr Panofsky suggests that the arms race is paced more by non-nuclear developments—delivery systems and so on—than by nuclear developments, and thus a ban on testing would not threaten US security. But Dr Philip J. Farley, Acting Director of the Arms Control and Disarmament Agency, said that “while seismic capability has improved, so has our understanding of the military potential of nuclear tests of lower yields”. And Dr Foster said that there are some cases in which nuclear tests involving an explosive yield of a half or a quarter of a kiloton would be militarily important. But if that is the official position of the Department of Defense, it would be a serious blow to chances of ever securing a test ban treaty because such small events could never be detected by seismic means.

The Administration witnesses all reaffirmed the US government's commitment to achieving a comprehensive test ban, provided it could be adequately verified. But, unless their unwavering insistence on on-site inspection is simply an initial bargaining position for the next round of the Conference of the Committee on Disarmament to be held in Geneva next month—which some observers are suggesting—the chances seem dim that a comprehensive test ban treaty will be signed before the tenth anniversary of the partial test ban treaty.

COMMISSION

How to Run Universities

THE Carnegie Commission on Higher Education has now turned its attention to the problems of how to strike a balance between the conflicting interests in higher education (*Governance of Higher Education*, McGraw-Hill, April 1973) and has in particular blessed the continuation of the institution of academic tenure. The report says that the issue is more of a challenge now than ever, partly because of the past growth and increasing diversity of universities and colleges, the pressures generated by the slackened pace of growth now in prospect, the demands of students and the conflicting views among the faculties of universities and colleges about the

function of higher education. The commission also includes enhanced public interest and reduced willingness to “accept authority” among the pressures on higher education. The problem, it says, is how to ensure a “reasonable” degree of independence from federal and state governments, separation from party politics, freedom for faculty members and faculty influence on academic affairs.

Among the commission's recommendations are the following:

- Where universities derive their support from public funds, there should be a general understanding between donors and recipients about the need that financial control should extend only to the outlines of academic policy. Budgets, for example, should not be defined in line-by-line items.
- Governing boards of publicly supported institutions should not include elected officials, especially those with financial powers, while the members of boards appointed, for example, by state governors should be screened in advance for suitability. At least some board members should be nominated for service by faculty, students and alumni.
- The commission has found that a majority of teachers in higher education

is now in favour of collective bargaining and almost half of a representative sample considers that strikes may now be legitimate in certain circumstances. It asks that all colleges should conform to the standards defined by the American Association of University Professors in 1972, which assert the importance of collective bargaining in higher education but which also draw attention to the special needs of universities and colleges. Those colleges in which collective bargaining is at present outlawed should be reformed.

SPACE

Skylab in Trouble

THE entire future of the Skylab project hangs in the balance this weekend with the failure on Monday of this week of the solar panels on the space station. These panels, which should produce in all about 21 kilowatts of electricity, failed to open when signals were sent from Earth although four other solar wings which provide power for controlling the optical telescope attached to Skylab are working satisfactorily.

The Skylab crew was due to begin work in the laboratory on Tuesday, but following the failure of the power system the launch of their Saturn 1B was put off until next Sunday (May 20). This allowed the mission planners time to assess whether there was any point in sending up a crew to a spacecraft with only half power. One question which was asked was whether the crew could reactivate the solar panels once they had arrived. But Mr Walter J. Kapryan, launch director at Cape Kennedy, said on Monday that the astronauts could do nothing to correct any malfunction in the solar panels. In particular Mr Kapryan emphasized that the panels could not be made operational by a space walk.

There are no firm plans for any Skylab missions after the present one and it is unlikely that Congress will feel generous enough to provide NASA with increased funds if the present mission has to be aborted.

Partly because of this, there seems a good chance that NASA will proceed with a more limited Skylab mission even if the power fault is not rectified.

There are four chief objectives of the Skylab mission. First, it is meant to determine the ability of people to live and work in conditions of weightlessness for extended periods. Second, the mission is to make observations with the optical telescope which are not possible from Earth. Third, to develop improved techniques for surveying the resources of Earth from space. Fourth, other experiments which are of particular interest if carried out in zero gravity and outside the atmosphere.

Alice in Eco-land Again

“THE Sierra Club magazine *Bonanza*,” said Alice, “wants no more sheep to be raised because the sheep farmers are killing coyotes.”

“Quite right,” said the Mad Hatter. “The sheep must go. The coyotes are native Americans. They lived on the range land before the sheep came.”

“But don't coyotes eat sheep?” asked Alice.

“They do,” said the Hatter, “but mutton fat is very high in cholesterol. It is not healthy for elderly coyotes who are subject to coronary disease. They should eat deer and rabbits, which are rich in essential unsaturated fatty acids.”

“What did you say?” asked the March Hare.

“I didn't mean you,” said the Hatter. “You are too tough.”

“Where shall I be able to get wool to knit sweaters?” asked Alice.

“You might try shearing a coyote,” said the Hatter. “They will become very tame when the sheep leave.”

THOMAS H. JUKES,
*University of California,
Berkeley, California*

NEWS AND VIEWS

Double Helix in Single Crystals

THE crystal structure of the dinucleotide phosphate adenosyl-3',5'-uridine phosphate (ApU) described by Rosenberg *et al.* on page 150 of this issue of *Nature* can be regarded as the "missing link" in nucleic acid stereochemistry. The crystal contains two molecules per asymmetric unit which interact with each other to form a segment of double helix two base pairs long. Each adenine is paired with a uracil and the pairing is of the type proposed for DNA by Watson and Crick; the helix is right-handed with the two sugar phosphate strands running in opposite directions so that there is an approximate two-fold axis relating the two molecules in the asymmetric unit. This two-fold axis is, however, local to the asymmetric unit and is not a crystallographic symmetry element. The stereochemistry of the sugar-phosphate chain is very similar to that determined for a variety of synthetic and naturally occurring two-stranded RNAs from X-ray diffraction analyses of crystalline fibres.

The similarities between the torsion angles observed in single crystals of nucleic acid components, and those determined in fibre diffraction analyses of nucleic acids themselves have been noted by several workers. This analysis of ApU puts the final touches to such correlations by revealing a structure of a nucleic acid component which not only has the preferred torsion angles characteristic of nucleosides and nucleotides in single crystals but which also looks like a nucleic acid double helix. As the authors rightly claim, it is the double helix at atomic resolution.

Perhaps the most important feature of the structure of ApU is that the base pairing is of the Crick-Watson type. This is the type of base pairing proposed as the basis for molecular recognition in, for example, replication, transcription, codon-anticodon interaction, and for all the structures of naturally occurring and synthetic two-stranded nucleic acids analysed by X-ray fibre diffraction. It is not, however, the form observed in mixed crystals of adenine and thymine (or uracil) bases, nor in the mixed crystal of the nucleosides adenosine and 5-bromouridine. In these crystals pairing through hydrogen bonding of adenine with thymine is observed but it is of the "Hoogsteen" rather than the Watson and Crick type. If the Hoogsteen pairing had been observed in ApU no doubt the analysers of nucleic acid fibres could have retreated and regrouped, but it is a relief to know that this is not necessary.

With the many pearls offered so obviously in the ApU analysis it would be only too easy to overlook many other features of considerable interest. The unit cell contains twenty-six water molecules; when the final analysis locates these accurately their stereochemistry should contribute greatly to understanding of preferred patterns of hydration on nucleic acid double helices and hence to models for hydrophobic stabilization. The binding of ions to nucleic acids is of considerable biological and stereochemical interest. In ApU there is one sodium ion per molecule. The two ions in each asymmetric unit occupy distinct sites. One is complexed between phosphate groups, but the other lies in the minor groove

of the DNA helix with octahedral coordination to two of the uracil oxygen atoms and to water molecules. Clearly this latter, rather unexpected type of interaction will stimulate a great deal of physico-chemical interest.

The structure of ApU is given added interest by the simultaneous determination in the same laboratory of the structure of the dinucleotide phosphate guanylyl-3',5'-cytidine (GpC) (Day *et al.*, *Proc. US Nat. Acad. Sci.*, **70**, 849; 1973). GpC also crystallizes as a double-stranded fragment but in this case the two-fold axis relating one GpC molecule to the other is a crystallographic symmetry element. The base-pairing is of the Watson-Crick type and, as for the structure of ApU, the conformation of the double-helical fragment is very similar to that determined by X-ray analysis of crystalline fibres of two-stranded synthetic and naturally occurring nucleic acids. Again the structure is heavily hydrated with thirty-six water molecules per unit cell.

These studies emphasize the value of single crystal studies of monomers and oligomers in the structural analysis of macromolecules. Increasingly it is being recognized that not only covalent bond geometry but also orientations about single covalent bonds and patterns of intermolecular interaction are strikingly similar in single crystals of macromolecular components to what they are in the macromolecules themselves. As a consequence very precise information obtained from highly refined structures of small molecules can be used in stereochemical analyses of large molecules in which attempts are made to correlate biological, chemical and physical information within a single molecular model.

W. F.

Invoking Black Holes

ELEMENTARY accounts of the scientific method often stress the way in which the observations of some unexplained object are built up so that a theoretical model can be inferred from them, as for example in the way the neutrino was invented to explain observations of β -decay. But there are spectacular counter-examples in which the solution came first and the problem which it fitted was found afterwards. The way in which the positron was found to fit the Dirac theory springs to mind. An astronomical example might be the neutron star. This object was shaken by Fritz Zwicky from what he called his morphological astronomical kaleidoscope, a way of permuting all possible combinations of matter into new objects. It was also invented by Oppenheimer and Volkoff in 1939 as a simultaneous solution of the equation of hydrostatic equilibrium of a self-gravitating mass and an equation of state for a degenerate material made up of neutrons. It was more than 30 years before an astronomical problem was found which appeared to require the neutron star for its solution—the radio and X-ray pulsars.

Of these the X-ray pulsars have provided the most clues

to their nature, for it is found, by observing the Doppler shifting of their periods and the way in which they are regularly eclipsed, that they are components of double star systems of small separation. In at least one case, known as Hercules X-1, the second star of the system is also known as an optically variable star, HZ Herculis. It has thereby become possible to deduce the mass of the X-ray pulsar in this system, which turns out to be about 0.5 of a solar mass. The significance of this result is that the simultaneous solution of the equations of hydrostatic equilibrium and of state for degenerate fermions is possible only for a restricted range of self-gravitating masses, whose upper bound (known as the Chandrasekhar limit) lies near 2 solar masses. The observed mass of the Hercules X-1 pulsar falls within the allowed range and gives confidence in the idea that it is a neutron star.

Not all X-ray binary stars can be described as confidently as this. Cygnus X-1 is the prototype of the difficult ones. Its soft X-ray flux was discovered by the Uhuru satellite to vary rapidly, but not periodically like a pulsar. The rapidity of the variations extends at least to the resolution time of the Uhuru satellite, namely 56 milliseconds. It is often said that this proves that the star responsible for the X-ray variations must be less than 56 light-milliseconds across, that is, less than 0.03 solar radii. If the X-radiation comes from gas, gravitationally compressed as it falls to a star's surface, and heated to X-ray emitting temperatures, as was proposed generally for galactic X-ray sources by Burbidge and Prendagast in 1967, then the X-ray emitting region envelopes the star and the star is indeed small. But the X-ray emitting region may actually be localized, tied to a star of arbitrary size.

Can one say anything more definite about this star? Cygnus X-1 is identified optically with a binary star system known as HDE226868, of which only one component is seen. It is a B-type supergiant star. The mass of its invisible companion is more than 10 solar masses, far above the Chandrasekhar limit. The companion is therefore not a self-gravitating mass of fermions, neither a white dwarf nor a neutron star. There are, in fact, normal stars of this mass, whose light would be swamped by the

large output from the supergiant, but if one is committed to the idea that the X-radiation is from compressed gas falling from the supergiant onto the invisible companion, one is forced to exclude a normal star as not having an intense enough gravitational field, and to speculate that the companion is a black hole. Indeed, as a lone black hole is one of the most difficult of all objects to detect, predictions about their appearance have concentrated on their effect on surrounding matter, so that it was pointed out by Shklovsky in 1967 that in the search for a black hole, one would look for a star affected gravitationally by an unseen companion, close enough to draw in matter from the normal star and emit X-rays. This could be a description of Cygnus X-1, published several years before its details were known, and it is not surprising that speculation about the nature of Cygnus X-1 has proceeded on the assumption that it is the first known example of a black hole.

As this account should have brought out, however, this conclusion is based on the facts interpreted by the theory of gravitationally compressed gas as the source of X-ray emission. Alternative models must be examined, if only to play the devil's advocate in testing the right of Cygnus X-1 to be called a black hole.

Such an alternative model was proposed by Bahcall, Kulsrud and Rosenbluth in *Nature Physical Science* last Monday (243, 27; 1973). They propose that the Cygnus X-1 binary system consists of two normal stars whose magnetic fields are interlinked and wound up by their orbital motion. The magnetic field breaks and reconnects at weak points with energy dissipation as X-radiation and so on, in a manner reminiscent of solar flares. As in the idea of gravitational compression, the X-radiation is powered by the gravitational field of the stars, so there is plenty of energy available for conversion, but the radiation arises from local regions in the magnetosphere of the binary star system. Random bursts of emission from these regions would cause the fluctuations observed in the X-ray flux.

If this model is substantiated, perhaps by the two observational tests which the authors themselves propose, then the problem to which black holes are an eager solution has yet to be found.

From a Correspondent

NUCLEIC ACIDS

Sweat and Serendipity

from our Molecular Biology Correspondent

ONCE more Sanger has produced an ace from his sleeve, and with that effortlessly inexorable air that suggests—as Disraeli in his exasperation said of Gladstone—that God had personally secreted it there. He describes with his colleagues (Sanger *et al.*, *Proc. US Nat. Acad. Sci.*, 70, 1209; 1973) a freshly minted method for sequencing DNA, and its application to a bacteriophage. The luck that attended their first foray into the sequence of R17 phage RNA has not deserted them, for they seem again to have hit on an interesting region between two cistrons; they report the sequence of a tract of fifty nucleotides, with of course another fifty on the opposite strand thrown in for nothing.

The new methods depend on first making a primer for copying the minus strand of the DNA, using the plus or "sense" strand as template, with DNA polymerase of *Escherichia coli*. Taking advantage of the known sequence of the principal coat protein, an oligodeoxynucleotide containing the codons for a presumed initiation point was synthesized (by what are now well established, if exacting, synthetic routines). With f1 phage DNA as template, the octanucleotide primer starts the synthesis of a new chain, the first eight nucleotides of which are thus known by definition. The next step was to omit from this reaction mixture one or more of the nucleoside triphosphate monomers. The oligomeric product is then separated by chromatography on ion-exchange paper, using Sanger's "homochromatography" technique, whereby oligonucleotides are displaced according to size by a front of mixed fragments of a non-radioactive digest sweeping through them, in the second dimension. The spots are subjected to nearest-neighbour analysis and depurination to determine their sequence, though the direction of displacement of each successive oligomer spot relative to that of its neighbour in the chromatogram practically allows the sequence to be read off by inspection. If only ATP and TTP are present in the reaction mixture, no further products appear after addition of six nucleotides to the primer. It follows that the seventh must be a G or C. If CTP is included, another six nucleotides are added before the presence of a G in the sequence brings the polymerization to a stop.

Beyond this point a different technique has to be applied, and here Sanger and his colleagues make use of an observation of Berg's that the DNA polymerase in the presence of manganese in place of magnesium will incorporate ribonucleotides. If then, for example,

riboCTP is included in the monomer mixture, the product will contain a ribose wherever a C occurs in the chain, and will accordingly be labile to pancreatic ribonuclease at each of these points. With f1 DNA, in the chosen conditions, this strategy produces seven prominent ribonuclease fragments, which were sequenced by the methods developed earlier. Since the enzyme does not run at uniform rate along the sequence, the polymerization product at a given time contains segments of different lengths, each terminating in a residue that the enzyme finds relatively unpleasing. These products were separated by the "homochromatography" method, and analysed for their content of ribonuclease fragments. This allowed the order of the seven fragments to be established, and so the sequence of the first fifty residues synthesized by the enzyme.

The first fact to emerge is that initiation had not occurred at the expected point, and indeed there is some evidence of an error in the reported coat protein sequence at this position. Rather, the fifty residues appear to encompass an intercistronic region in the complementary sequence, which is also that of the messenger, and which contains three termination codons, all mutually in phase, just as was found at the end of the coat protein cistron of R17 phage RNA. On either side would be the message for a protein ending in gly-phe-ile-ala, and another beginning formylmet-val. This reading, of course, is not yet proven, for the phase could be taken differently. A feature of the nucleotide sequence is that it is remarkably rich in T residues, and contains several short repeated sequences, that gives support to the theory whereby the early evolution of DNA involved sequence duplication, followed by mutations to generate useful messages. There is a notable homology in part of the f1 sequence with that of an icosanucleotide from ϕ X 174 DNA, which represents a ribosomal and binding site, and contains the initiation sequence for a structural protein.

Meanwhile the precepts of Sanger and his associates are being applied to many of the central problems of molecular biology. Murray (*Biochem. J.*, **131**, 569; 1973), working with λ and 424 phage DNA, has used the method of radioactive end group labelling with polynucleotide kinase to obtain striking nucleotide maps from these species. Many oligonucleotides were sequenced, and the functionally important terminal sequences were determined. The two phages were found to be identical in this respect, which provides the physical basis for their ability to form mixed dimers by way of their cohesive unpaired ends.

On the RNA front, Rensing (*ibid.*,

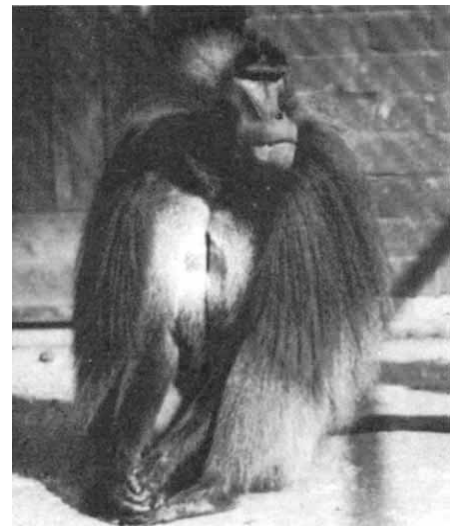
593) has produced a new sequence of seventy-three residues from R17 RNA, which is not related to the coat protein genes. It can be read through in one frame from end to end, and is remarkable in that it contains two runs of twenty-three and twenty-four residues, the sequences of twenty-two of which are identical. What it codes for is not established, for the sequences of both the A protein and the polymerase are unknown, and only the coat protein, the RNA sequence for which is now fully determined, has a known sequence. In a further report, Rensing *et al.* (*ibid.*, 605) give the sequence of another fragment of thirty-three nucleotides, as well as two other pieces identified as arising respectively from the start of the A-protein cistron and just before the ribosome binding site that precedes the coat-protein cistron. One of the fragments especially has the potential to form a hairpin of 11–12 successive base pairs.

PRIMATES

Fossil Baboons of Africa

from a Correspondent

THE gelada baboons of Ethiopia are no more than a surviving remnant of a once-thriving group of specialized grassland monkeys, according to Jolly, who has made an exhaustive study of large African Plio-Pleistocene fossil baboons generally attributed to the genus *Simopithecus* (C. J. Jolly, *Bull. Brit. Mus. (Nat. Hist.) Geol.*, **22**, 1; 1972). Indeed, Jolly feels that these fossil forms should be placed as a subgenus in the same genus as the living gelada baboon (*Theropithecus gelada*), as an indication of their close relationship. This sug-



Gelada baboon (photo: Zoological Society of London).

gestion is based on the hypothesis that both the fossil *Simopithecus* and the modern geladas share many adaptations for an open-country grassland niche, with grass blades, seeds and rhizomes—picked by hand—providing the bulk of the diet. *Simopithecus* is thought to have resembled the gelada in that it rarely, if ever, utilized trees, because study of various limb fragments indicates extreme adaptation for terrestrial locomotion (short, stubby digits; robust skeleton; poorly developed hallux; arms and legs similar in length).

The general picture of a large bodied, ground-living form specialized for feeding on small objects is confirmed by detailed study of the skulls, jaws and teeth of *Simopithecus*, which are richly illustrated in Jolly's monograph. When compared with typical baboons (genus

Testosterone and Ovarian Function

WITH the development of mammalian genetics the growing range of mutants available is becoming valuable for answering fundamental problems outside genetics. In *Nature New Biology* next Wednesday (May 23) there is a further report on the testicular feminization or *Tfm* mutant of the mouse, which in the hands of Ohno and his colleagues has already proved of great interest.

This X-linked gene is interpreted as a non-inducible mutation of the regulatory gene involved in the response of target organs to testosterone, and animals affected with it lack all response to androgen. The affected animals are usually genetically male, *Tfm/Y*, and have testes. Ohno *et al.* have now found six affected animals which were chromosomally XO, that is *Tfm/O*, and therefore genetically female and with ovaries. This has made it possible to test whether testosterone has any function in female reproduction. The ovaries of the

youngest *Tfm/O* were normal, but the five older animals showed rapid deterioration of the ovaries, best described as precocious luteinization of follicles. It thus seems that in female mice a response to testosterone is essential for normal ovarian function.

The X linkage of the *Tfm* gene is of further interest in this context, because mammalian oocytes also require the presence of two X chromosomes for completely normal survival. Could the normal allele of the *Tfm* gene be one of the genes whose function in double dose is needed? The degeneration in *Tfm/O* was indeed similar to, but more severe than, that seen in $+/O$ ovaries. Further work will, however, be necessary to answer this question definitively, because the work of Ohno *et al.* does not yet exclude the possibility that the effect in *Tfm/O* ovaries was more generally systemic, involving hormonal interactions and the hypothalamo-pituitary axis.

Papio), *Simopithecus* and modern geladas show a complex of characters which indicate extensive adaptation to grass eating: the cheek-tooth crowns are more complex, and the molars and premolars have a relatively large surface area, whereas the incisors (used for extensive food preparation in *Papio* species) are very small. The lower jaw has a high, vertically ascending ramus, and the contours of the braincase indicate well-developed temporal musculature for mastication. Finally, there is some indication that the third molars may have erupted relatively late in *Simopithecus*, thus extending the active life of the cheek teeth.

Jolly shows, however, that it is misleading to refer to all *Simopithecus* as "giant baboons". The two recognized species, *Theropithecus* (*Simopithecus*) *oswaldi* and *T. (S.) darti*, both exhibit a fair range of body size; the smallest known individuals are comparable in size to modern *Papio anubis* (olive baboon), and the largest known fossil males were probably as big as a female gorilla. As in the modern gelada, there was considerable sexual dimorphism, and males were apparently considerably heavier than females.

Apart from providing a detailed account of the known fossil material attributable to *Simopithecus*, Jolly also considers the geographical range and timespan covered by the fossils. *Simopithecus* was obviously widespread in East and South Africa during the late Pliocene and the bulk of the Pleistocene, occurring at presumed "waterside" sites. The earliest known fossils date back to about 5 million years ago, and extinction of the fossil subgenus seems to have occurred about 50,000 years ago. This disappearance of a once-successful species is traced to human hunting and ecological competition. Jolly postulates that the modern gelada represents a highland branch of a Pliocene ancestral stock which also gave rise to lowland forms of the subgenus *Simopithecus*. At some time in the late Pleistocene, human activity may have led to the extinction of the large-bodied lowland forms, leaving the highland geladas (temporarily?) relatively unscathed. Jolly does not believe that overhunting led directly to the extinction of *Simopithecus*. Instead, he suggests that human activity upset the delicate balance of ecological separation between *Simopithecus* and other baboons (*Papio* species), and this in turn led to the extinction of the grass-eating *Simopithecus*.

Jolly's account attains a wider significance in that the dental adaptations for small-object feeding in *Simopithecus* and the gelada may provide a model for dietary adaptations associated with dental changes in the early stages of human evolution (Jolly, *Man (Lond.)*, NS, 5, 1; 1970).

NUTRITION

How Much Vitamin C?

from a Correspondent

FOR the past several years Linus Pauling has vigorously maintained that people benefit, indeed need, perhaps more than ten times the minimal daily requirement of vitamin C that was established many years ago, if they are to be really healthy. He has in particular argued that by taking what are by conventional standards very large daily doses of ascorbic acid people can avoid such diseases as the common cold and influenza. As Yew points out in the current issue of the *Proceedings of the National Academy of Sciences* (70, 969; 1973), sceptical nutritionists "who ignore this suggestion or have merely used rhetoric to refute it appear to accept axiomatically two crippling but time-honoured assumptions, first, that ascorbic acid functions merely to prevent 'scurvy' and, second, that within a species a narrow range of needs must of necessity exist".

Nobody of course denies that the current recommended daily minimal doses are insufficient to prevent scurvy; the question is whether a much larger dose not only prevents scurvy but also promotes good health and development of human beings. Yew claims that very little information about the amount of ascorbic acid needed to keep humans healthy has been obtained in the 41 years since the vitamin was identified. In an attempt to obtain some comparative data he fed a scorbutic diet supplemented with ascorbic acid at four differ-

ent levels (0.05, 0.5, 5.0 and 50 mg/100 g of body weight per day) to populations of healthy guinea-pigs. He then measured the response of animals eating these various amounts of ascorbic acid to surgical stress, recovery from anaesthesia and scab formation and wound healing. His conclusion is that young guinea-pigs need about 5 mg per 100 g body weight per day and under stress the requirement is even higher. These amounts are much higher than anybody has supposed, even though commercial guinea-pig chow contains enough vitamin C to give animals about 3.3 mg per 100 g body weight.

It is perhaps naive simply to extrapolate from these data to the human need for this vitamin, but if the extrapolation is made a 30 kg child would need 1,500 mg of ascorbic acid daily compared with the US Food and Nutrition Board's recommendation of 40 mg per day. Yew's point is simply that it is now up to those responsible for setting vitamin requirement standards to get to grips with the problem and try and discover just how much vitamin C young people do need to develop to their full potential. He repeatedly throws out this challenge saying, "The burden of proof must now shift to the medical scientists who are really concerned about the health and physical condition of young people to show that considerations that apply to young guinea-pigs do not apply to young people." And broadening the issue Yew concludes that "if this gross uncertainty in human requirements for ascorbic acid prevails in nutritional science can there not be comparable uncertainty with

A Three Point Landing

MUCH scientific sleep has been lost over the problem of how transfer RNA binds to the aminoacyl synthetases and where in their specificity to these enzymes resides. An attractive answer to these problems is provided by Dube in next Wednesday's *Nature New Biology* (May 23).

Dube, working with *Escherichia coli*, isolated complexes of tRNA^{met} and the methionyl-tRNA synthetase and treated these with ribonuclease T₁. Fingerprints of the resulting digests revealed that four oligonucleotides were present but in low yield in comparison with uncomplexed tRNA. These oligonucleotides could be unambiguously assigned to the anticodon loop, and the 3' side of the anticodon arm, the extra arm and to the 3' side of the stem. It was inferred that binding to the synthetase protected certain G residues in these regions of the structure from attack by the enzyme.

This conclusion suggested to Dube that these regions were on the same side of the molecule as opposed to the TuC and DiHU loops. This suggestion

fitted in nicely with the structure of tRNA^{phe} proposed by Kim *et al.* (*Science*, 179, 285; 1973) from X-ray crystallographic evidence. The anticodon loop and the 3' end are at the two extremities of an L in this model, and if the enzyme is also to interact with the extra loop it must have three binding sites located on an arc which fits into the angle of the L. Recent work by Schulman (*Proc. US Nat. Acad. Sci.*, 69, 3594; 1972), who chemically modified G₄₆ (in the extra loop), G₇₁ (in the 3' stem) and C₃₅ (in the anticodon loop), supports this notion, for these modifications led to complete inactivation of tRNA^{met} with respect to methionine acceptance. It is of interest that these residues are conserved in tRNA^{met} which is aminoacylated by the same enzyme.

Dube finally suggests that a three point attachment to an arc shaped active centre may be the key feature in tRNA recognition and that the variable extra arm may play a vital part in this process.

respect to other vitamins, such as vitamin A and vitamin D?" Yew at least is firmly in Pauling's camp and it will be interesting to see what response there is to his provocations.

MOLECULAR BEAMS

Scattering Branches Out

from a Correspondent

MEMBERS of what was described by Professor D. R. Herschbach (Harvard University) as the "lunatic fringe", who first reported molecular beam scattering results at the Faraday Discussion on inelastic collisions in 1962, were in a confident mood at the Chemical Society Faraday Division general discussion on molecular beam scattering held in University College, London, from April 16-18. This confidence stemmed from new techniques which make it possible to study some of the problems in chemical reaction and energy transfer which arise in the main stream of chemistry. These developments include the liaison, if not yet the marriage union, of spectroscopic and scattering methods, as in the laser-induced beam fluorescence experiments described by Dr R. N. Zare (Columbia University), as well as the reports from many laboratories describing experiments with a broad range of atomic and molecular species. This latter feature was in particular contrast to the position at the last Faraday Discussion on this topic in 1967 when beam experiments had to include at least one alkali atom because of detection difficulties with other species.

The measurement of intermolecular forces by beam methods was one of the topics discussed at the conference; interest here is now centring on the forces between energetically excited or otherwise chemically labile species. Unfortunately there are few quantum computations of such potential surfaces with which these measurements may be compared.

Professor J. P. Toennies (Max-Planck Institute, Göttingen) described measurements of the angular distribution of rotationally excited H_2 resulting from collisions with fast Li^+ ions. The distribution of rotational states was resolved by measuring the associated change in the velocity of the Li^+ ion using a time-of-flight method. This is a new achievement for, until recently, techniques were insufficiently sensitive to permit any information about the angular distribution to be obtained. Interestingly, the results presented were not in accord with the rather precise quantum calculations available for this system.

Most of the meeting was, however, concerned with the use of molecular beam methods to explore the dynamics

of chemical reaction. Professor D. R. Herschbach (Harvard University) discussed the results of experiments involving four participating atoms such as $CsBr + ICl \rightarrow CsCl + IBr$. Depending on the precise reactants, the angular and energy distributions found for the product varied from those expected from a long-lived collision complex decaying with a statistical distribution of the energy into the product molecules, to those characteristic of a specific short-lived interaction. The transition between these two types of behaviour correlate with the shape of the complex predicted by molecular orbital theory. Reaction by way of a long-lived complex was also reported for systems such as $F + C_2H_4 \rightarrow C_2H_3F + H$ (Dr Y. T. Lee, University of Chicago). These were especially interesting because the energy distribution did not follow that expected statistically from the RRKM model for unimolecular reactions. These results suggest that the assumption inherent in this model, that chemical reaction is slow by comparison with a rapid internal randomization of the reaction energy in the complex, may be incorrect. This possibility was discussed by several speakers and the suggested use of information theory methods to characterize the degree of non-statistical behaviour found favour. Further light on this problem came from Monte Carlo trajectory calculations extended over the life of four-atom complexes (Na Br KCl); for this strongly coupled system, the statistical approximation seemed fairly good.

The reaction between alkali metal atoms and alkyl halides, a molecular beam "chestnut", continued to be of interest to theoreticians and experimentalists alike, the latter still comfort-

ably in the lead. The quantity of information available concerning these reactions is now so large that it is extremely difficult to find potential surfaces capable of reproducing, using Monte Carlo calculations, all the observed features. A successful surface would now be almost uniquely constrained.

The conference concluded with a summary contribution from Dr J. C. Polanyi (University of Toronto), who related present achievements and future prospects to the pioneering work in the 1930s of his father, M. Polanyi, who was present in the audience.

TECHNIQUES

Archaeological Dating

from a Correspondent

SUBJECTS of interest to both archaeologists and scientists were discussed at the meeting on archaeometry and archaeological prospection in the Clarendon Laboratory, University of Oxford, from March 29 to 31.

Descriptions of new developments in instrumentation for geophysical survey based on electromagnetic and resistivity principles were described emphasizing the greater sensitivity and general portability now attainable. Methods of rapidly displaying the results of the measurements for archaeological evaluation were explained by Drs E. T. Hall (University of Oxford) and I. Scollar (Bonn Museum) who showed the desirability of presenting data as punched paper tape suitable for use with a computer programmed for pattern recognition and/or image enhancement.

It was natural, at Oxford, that much

Messenger RNA Activity in β -Thalassaemia

HUMAN β -thalassaemia has been characterized by decreased or absent synthesis of the β -globin chain in erythroid cells and the defect has been localized at the polysome level. In *Nature New Biology* next Wednesday (May 23) Dow *et al.* report their studies of the activity in a cell free system of mRNA isolated from polysomes or whole cell lysates of the blood of patients exhibiting different levels of β -chain synthesis.

Using a Krebs II ascites cell free system with rabbit reticulocyte ribosomal initiation factors, Dow *et al.* demonstrate that addition of 10S RNA isolated from polysomes of non-thalassaemic cells led to the synthesis of both α - and β -chains in relatively equal amounts (α/β ratio of 0.79-1.0). This compared well with the α/β ratio of whole blood cells. When, however, 10S RNA from polysomes of β -thalas-

saemic blood was tested in the cell free system, a marked decrease in β -chain synthesis occurred (α/β ratios 1.8-3.6). Again the ratios were similar to those obtained with whole cells. The results were the same when 10S RNA was extracted from whole cell lysates rather than polysomes. Because the ratio of α/β chain synthesis is the same whether extracted RNA or whole cells are used, it is probable that mRNA, if present in β -thalassaemic cells, is either decreased or abnormal.

Previous workers who arrived at this same conclusion used a pool of cells of two β -thalassaemic patients or the cells of siblings or an individual patient as the source of mRNA. Dow *et al.* now confirm this result in a number of unrelated patients exhibiting a range of β -chain synthesis including no β -chain formation.

time was devoted to the varied aspects of thermoluminescence (TL) dating. In a critical review of the theories of the phenomenon Professor G. J. Garlick (University of Hull) pointed out that in fundamental studies difficulties in deducing trapping parameters have arisen and that non-thermal leakage of trapped carriers has been found. This leakage, which is caused by overlap of wave functions of trapped carrier state and ground state, affects the limits of dating by this technique. The intensive investigation of TL dating, which promises so much, was shown by several contributors. A rather large array of factors, for at least some of which corrections must be made before one can reduce the errors of TL dates to small proportions, were presented, but the overall impression was that the difficulties would be overcome. Dr A. G. Wintle (University of Oxford) reported that feldspars, zircon and fluorapatite all lose some artificially induced TL from the high temperature part of the glow curve after some days storage. Fortunately, quartz and limestone do not exhibit this "fading" effect. Dr V. S. Desai (University of Oxford) showed that pottery saturated with water attenuates the escape of radon, and subsequent members of the uranium-238 decay chain, the isotopes of which are responsible for an appreciable fraction of the radiation dosage received by the pottery. Thus, changes of water content and the porosity of the pottery could modulate the dose rate received as was pointed out by Dr V. Mejdahl (University of Copenhagen); and Dr J. Huxtable with Dr M. J. Aitken (University of Oxford) demonstrated that the radioactive impurities themselves could be leached in slightly acidic conditions giving yet another potential source of error in pottery during centuries of burial.

The magnitude of the supralinearity correction routinely applied during TL dating by the fine grain method was shown by S. J. Flemming (University of Oxford) to vary, in many instances, with the pottery's previous radiation history, and consequently affects the error in the date. Dr D. W. Zimmerman (University of Washington, St Louis) explained how these errors could be eliminated in certain special cases. He required that the inclusion in the archaeological ceramic itself was highly radioactive, as opposed to the normal case of matrix radioactivity. The zircon or apatite should have a sufficiently large internal dose rate of α -particles to swamp any environmental γ -dosage, and this also would not be attenuated by the presence of water. Such a specimen may be used for authentication purposes even after the pottery has been X-rayed in previous analyses, a process which would prob-

ably invalidate the standard TL authentication methods.

Dendrochronology was discussed at some length during one session. The method is relatively new in Britain though studied for some 70 years in the United States. Dr J. M. Fletcher (University of Oxford) presented the results of his two years' work on a series of oak trees, supplemented by timber from nearby mansions, panels from Tudor portraits and some large chests in Westminster Abbey. He has been able to construct a reference tree-ring curve back to AD 850. Similar impressive work by the palaeoecology laboratory at the Queen's University, Belfast, was described by Dr A. G. Smith. In four years they have assembled a series of floating tree-ring chronologies extending for about 7,000 years as attested by radiocarbon dating. This was accomplished by cross-linking oaks and pines preserved in some of the peat bogs in Ireland. It is hoped that the missing sections will soon be discovered and then a chronology rivalling that of the bristlecone pine will become available.

A spirited discussion following two contributions on methods of correcting radiocarbon dates ensued and it was postulated that two "types" of calibration curve were possible, one for explaining geophysical perturbations of atmospheric radiocarbon and another for the correction of archaeological

dates. Dr H. McKerral (Scottish National Museum, Edinburgh) examined in detail corrections in the early bronze age of Britain and concluded that corrected dates were much later than expected on historical grounds. A statistical investigation by Professor C. Renfrew (University of Southampton) and Dr R. M. Clark (University of Sheffield) of bristlecone pine calibrated and historically dated Egyptian samples indicated that the errors of the radiocarbon dates had been underestimated or that the assigned calendar dates of some of the samples were in error, or both. Calibration curves fitted by computer indicated, however, that the Egyptian and the bristlecone pine data are compatible within the relevant time period. The fear initiated among some archaeologists by a "red herring" in a recent review article, that the bristlecone pine calibration data might be distorted by as much as 1.5 per cent by carbon-14 produced *in situ* in trees growing at high altitude by the action of cosmic ray neutrons with nitrogen fixed in the cellular structure of the wood, was allayed by Drs D. Harkness (Scottish Research Reactor Centre, East Kilbride) and R. Burleigh (British Museum) who reconsidered the theoretical predictions. They suggested that the amount of radiocarbon thus produced is below the limit of measurement, and so could not affect the calibration curve.

A New Protein Controlling Cell Division

In *Escherichia coli* the completion of DNA replication is a prerequisite for cell division. It is known that protein synthesis is essential for cell division and, to date, two distinct periods of protein synthesis have been described, the first being required for the initiation of replication, the second taking place concurrently with replication. In *Nature New Biology* next Wednesday (May 23), Jones and Donachie describe a third period of RNA and protein synthesis which occurs at or subsequent to completion of DNA replication.

Jones and Donachie used a strain of *E. coli* which is able to resume RNA synthesis after treatment with rifampicin and removal of the antibiotic from the medium. They pretreated their cells in such a way that they became synchronized with respect to a single round of DNA replication and a single subsequent wave of division. Readdition of thymine after pretreatment led to a synchronous reinitiation of chromosome replication within 10 min. The replication was complete by 40 min and was followed 5 min later by cell division. Inhibition of completion of the first round of chromosome replication prevented cell division.

Addition of rifampicin up to 35 min after administration of thymine prevented most division but addition at 45 min had no effect on division. Addition of chloramphenicol at any time up to 40 min after thymine prevented all cell division. Later addition of chloramphenicol had no effect. Thus RNA and protein synthesis are required 5–10 min before division. RNA synthesis is not required at an earlier time, because if rifampicin is added at the same time as thymidine and subsequently removed (before the 5–10 min prior to division), the timing of division is unaffected. Furthermore, synthesis of this specific RNA and protein required for division can take place only after the replication of a late segment of the chromosome. Once fermentation has occurred, RNA and protein synthesis required for division can take place even after a 30 min delay.

These experiments therefore demonstrate the existence of a "termination protein" the synthesis of which is signalled by the completion of DNA replication and the function of which is presumably to act to prevent cell division before completion of chromosome duplication.

Great interest was shown in the description of Dr E. W. MacKie (Hunterian Museum, Glasgow) of his excavation of a stone platform near the large standing stone at Kintraw, Argyll. This, according to the theories of A. Thom, was the observation point of the megalithic midwinter solstice observatory in prehistoric times. Unfortunately, no artefacts were found but a petrofabric analysis of the stones of the platform is demonstrably similar to a platform known to be man-made and quite dissimilar to natural ones.

SOLID STATE

In Two Dimensions

from a Correspondent

A CALCULATION by Novaco (*Phys. Rev. A*, **7**, 678; 1973) provides strong support for an earlier suggestion that a single layer of helium atoms, adsorbed on a smooth surface at low temperature, behaves as a two-dimensional solid.

An adsorbed atom (adatom) is strongly bound to the surface of another material (substrate) by the so-called Van de Waals force of attraction. The adatom therefore finds itself trapped in a two-dimensional world where, if the substrate is smooth, it is entirely free to move in any direction parallel to the surface, but where motion in the third dimension, perpendicular to the surface, is rigorously forbidden. When many adatoms coexist on the same substrate, the normal concepts of kinetic theory may be expected to apply: each atom will possess a certain average speed, dependent on the temperature, and atoms will frequently collide with each other, exchanging energy and momentum; but all these processes will be occurring in two dimensions rather than the normal three. The sole function of the substrate is that of constraining the assembly to remain in two dimensions, it being regarded otherwise as completely inert.

Several different substrate - adatom combinations have now been studied, but particular attention has centred on helium adatoms because the Van de Waals force between a pair of helium atoms is so small that a low density assembly can be expected to behave as an ideal two-dimensional gas, a situation which is relatively easy to tackle theoretically. At higher densities, the adatoms, being more closely packed on the substrate, will have less freedom to move about, and so might perhaps be expected to form a two-dimensional solid. This latter point is by no means obvious, however, for three-dimensional helium does not solidify, even at zero temperature, unless a substantial external pressure is applied.

Very striking demonstrations of the general validity of these ideas have been

achieved by Dash and his colleagues at the University of Washington, who have measured the heat capacity of helium adsorbed on a form of graphite at temperatures of a few K. This substrate has the advantage, in addition to being very smooth, that a small volume of the material presents an exceedingly large area of surface for adsorption: their 12 cm³ cell contained more than 200 m² of graphite surface. The heat capacity of the substrate was therefore considerably less than that of the adsorbed film, which could then be measured with impressive precision. In earlier investigations they were able to demonstrate that, at low (that is, sub-monolayer) coverages, the helium atoms indeed display many of the properties predicted for two-dimensional gases, but their most recent work (Bretz, Huff and Dash, *Phys. Rev. Lett.*, **28**, 729; 1972) concerns the situation where the substrate is, in effect, completely covered with helium. To their surprise, they found that the heat capacity passed through a very sharp maximum at a temperature which depended on the two-dimensional density of the monolayer.

They tentatively attributed this phenomenon to a melting process: at temperatures well below that of the peak, the atoms would all be localized in some sort of two-dimensional lattice; whereas, above the peak, they would be able to move about freely, forming a two-dimensional liquid. Just as in the case of three-dimensional helium, the melting point would move to higher temperatures if the density of the two-

dimensional solid was increased by adding extra adatoms, consistent with the experiment. A surprising feature of their results was that, at temperatures well below the peak, the heat capacity of the two-dimensional solid corresponded to that of three-dimensional helium at a pressure of several hundred atmospheres. This seemed remarkable at first sight, for the "actual" pressure (that is, that of the real three-dimensional vapour in equilibrium with the adsorbed film) was negligibly small. A plausible explanation was put forward, however, in terms of the very strong attractive force between adatom and substrate, which might be able to pull many additional helium atoms down onto the surface even though it meant compression of an already complete monolayer.

Novaco has now put this suggestion to the test, theoretically, by calculating the densities and corresponding heat capacities which would be expected at very low temperatures, if the monolayer were indeed a close-packed two-dimensional solid. That his calculated values are in satisfactory agreement with experiment is encouraging evidence in support of the model. Unfortunately, the heat capacity measurements yield no information on the two-dimensional lattice structure and, indeed, cannot show unambiguously that the monolayer is solid rather than liquid. Novaco points out that a neutron scattering experiment, now in the planning stage, may perhaps yield definitive answers to these questions.

Radio Emission from Supernova 1970g

SUPERNOVA 1970g was a type II event which occurred in the external galaxy M101. In next Monday's *Nature Physical Science* (May 21) Goss and colleagues report observations of the supernova remnant made with the Westerbork Synthesis Radio Telescope (WSRT) at 21 cm and 6 cm and with the Max Planck 100-m instrument at 2.8 cm.

The observations were carried out during late 1970 and early 1971. Mapping at 21 cm took place during November, December and January; the resolution of the final map is 25 arc s $\times$ 30 arc s. Better resolution is achieved at 6 cm, of course, but at that wavelength the source was viewed only for one period of 12 h on January 26, 1971. But this observation does reveal a source of about 4×10^{-3} f.u. at the position of the supernova. The 2.8 cm observations, on the other hand, show no emission above 6×10^{-3} f.u. at the position of the supernova remnant.

Studies of the radio emission from this supernova are handicapped by its proximity to NGC5455, an HII region.

But between December 1970 and December 1971 the emission from that part of the sky increased by 6×10^{-3} f.u.; HII regions do not usually vary over that sort of timescale, and Goss *et al.* conclude that the variable radio emission may represent the first stages in the development of a radio emitting remnant.

Curiously, the observations reported now indicate a strong flux at 21 cm in February 1972, when Gottesman *et al.* (*Astrophys. J.*, **174**, 383; 1972) noted a disappearance of the source at 11 cm. Taking both observations at face value, this poses serious problems in defining a spectral index for the source.

As yet, it is too early for the observations of this young supernova remnant to provide convincing support for a unique theoretical model. The mechanism is probably non-thermal, but the radiation could be coming either from a region surrounded by the ejected material (perhaps even from a young central pulsar) or from outside the supernova shell and still produce the observed characteristics.

AGU

Geophysical Perennial

from our Geophysics Correspondent

TRYING to report adequately on the American Geophysical Union's annual meeting in Washington (April 16–20) is like trying to describe St Paul's Cathedral from a couple of picture postcards. An attendance of 2,500, with 1,200 contributions, makes it impossible to give anything other than a highly localized account, fortified somewhat by gossip.

This year there was a significant upturn (20%) in the number of papers presented. This appeared to be an across-the-board expansion, although obviously planetology, with several tens of papers on the Moon, Mars and the Allende Meteorite, profited particularly this year. Contributions on lunar geology were headed by one from Dr Harrison Schmitt, who was laconically described in the programme as "the first AGU member to visit the Moon". Dr Schmitt, of course, drew a big crowd but it was a matter of some disappointment that the other key speakers—Drs F. Gilbert (University of California San Diego) and C. Hosler (Pennsylvania State University)—had sparse audiences. Dr Gilbert's weighty approach to inverse problems, although not likely to be appreciated by the arm wavers, has an applicability well beyond the Earth structure problem to which it was first applied, and future geophysicists will ignore it at their peril. Dr Hosler's lucid account of experiments in weather modification deserved a bigger crowd not least for the many remarkable photographs he showed. It would be unfortunate if a trend were established away from such lectures. A not altogether desirable tendency seems to be emerging of the completely unstructured session in which several participants identified as working on the "Frontiers of Frontiers" talked (chatted might be a better word) about recent work with extensive interjection from the audience.

A most exciting development is the rapid advance being made in the discovery of criteria by which an earthquake may be predicted. Two distinct lines of research have proved fruitful. In the first, detailed seismicity maps of a region of the Earth are compiled and attention is paid to the aftershock activity from relatively large earthquakes. This probably delineates the region of slip. Frequently these aftershock zones do not overlap (at least in a substantial period of time) and this leads to the unsurprising conclusion that regions which have not recently been so delineated by aftershocks are most prone to rupture in the future. Drs J. Savino (Lamont-Doherty Observatory)

and R. Wesson (US Geological Survey) examined seismicity as a tool for prediction in Alaska and California. Dr Savino found that the Sitka earthquake of 1972 occurred in an identifiably higher risk region. Dr Wesson demonstrated that in California, before moderately large earthquakes, the numbers of small earthquakes rise. Dr W. Ellsworth (US Geological Survey) bravely went as far as to predict, on the basis of the above criteria, a magnitude 4.5 earthquake at 36° 40' N 121° 17' E (near Hollister) within the next few months, and the evidence certainly seems plausible.

The second approach to seismic prediction depends on some remarkable changes in the physical properties of rocks in the vicinity of some thrust-type earthquakes. In the 1960s Russians observed some apparently premonitory

signs of earthquakes in central Asia. Of these the most easily measurable was a change in seismic velocities of rocks in the vicinity of the fault. Dr Y. Aggarwal (Lamont-Doherty Observatory) reported the recent discovery of similar features before small earthquakes in New York State, and Dr J. Whitcomb (Caltech) described velocity anomalies before the San Fernando earthquake. Dr Whitcomb's results leave little doubt that it is the compressional wave velocity which changes—declining by about 20% and then returning to a normal value just before the quake. The region in which this effect occurred for the San Fernando earthquake seems to be particularly large, at least 50 km in linear dimensions. Dr C. Scholz (Lamont-Doherty Observatory) presented an attempt to unify many of the precursory phenomena now reported by Russians, Japan-

Upper Mantle Viscosity by Stokes's Law

STOKES'S method for determining the viscosity of a fluid must be familiar to anybody who has been through even the most elementary of courses in experimental physics. In the classic version of the experiment, a small sphere is dropped through an effectively infinite volume of the fluid, and the viscosity is calculated from a simple formula involving the sphere's radius, density and terminal velocity. On the face of it, the method has little application to the Earth's mantle; but in a fascinating analysis in next Monday's *Nature Physical Science* (May 21), Christoffel and Calhaem show how the same simple principles may be used to derive the viscosity of the upper mantle.

The falling body in this case is a piece of the Earth's lithosphere. Barazangi *et al.* (*Nature*, **242**, 98; 1973) recently suggested, on the basis of an analysis of intermediate and deep earthquakes and the associated seismic attenuation, that beneath New Zealand a fragment of the descending lithosphere has broken off and has now reached a depth of about 600 km as it sinks into the mantle ahead of its parent body. From the thickness of the lithosphere beneath New Zealand and the vertical and horizontal distributions of the deep earthquake foci, Christoffel and Calhaem conclude that the sinking fragment may be fairly regarded as a sphere with a diameter of 60 km—a sphere because, whatever the fragment's original shape, its corners will by now have been eroded by frictional heating.

To determine the velocity of the lithospheric fragment it is necessary to know when it broke off and how far it has fallen since then. Assuming that such a break would have visible effects at the surface, Christoffel and Calhaem equate the time of the break to the changes

in volcanic and tectonic activity which occurred in New Zealand 3.8 million years ago, at which time what is now the fragment would have been 380 km above its present position. This gives a velocity of 10 cm a year, assuming that the piece of lithosphere is falling under gravity and that there are no convection currents. The only other parameter required, the density of the fragment, was estimated by Adams (*New Zealand J. Geol. Geophys.*, **6**, 209; 1963) from surface gravity anomalies to be 0.05 g cm⁻³.

Putting these figures into the Stokes's Law formula gives a viscosity value of 3.1×10^{20} poise, a constant value which represents the effective viscosity of the upper mantle over the depth range 250–600 km and over a period of almost 4 million years. If, however, frictional heating causes partial melting at the surface of the fragment as it falls, the diameter used to calculate the viscosity may be too high; and if the medium through which the fragment is falling is not effectively infinite, the measured terminal velocity will be too low. The Stokes's method viscosity should therefore be regarded as a maximum. Even so, it is in good agreement with Gordon's estimate (*Geophys. J.*, **14**, 33; 1967) of effective viscosity at a depth of about 600 km and only slightly less so with the estimate made by McKenzie (*Geophys. J.*, **14**, 397; 1967). On the other hand, it is significantly lower than upper mantle viscosity values derived from seismic behaviour and from isostatic readjustment. But as Christoffel and Calhaem point out, seismic and isostatic methods involve either complex models or time scales quite different from those of plate motions, and the resulting viscosity values thus have less relevance to plate tectonic theory.

ese and Americans in terms of the development of dilatancy in strained rocks, flow of fluids into the dilated region, the hardening of the rocks in dilated form and ultimately the release of strain by the rise of pore pressure along the fault. Both Drs Scholz and Whitcomb drew attention to a very striking correlation between duration of precursory phenomena and size of earthquake. If the correlation holds good in the light of further study it seems that a magnitude 8.0 earthquake would give tens of years of advance warning. In spite of the many questions this work raised during the meeting, particularly about the extent of its applicability, it is clear that earthquake prediction has seen a significant advance in the last year.

The problem of mantle hotspots underwent little resolution during the meeting in spite of many papers on the subject. Based on a suggestion by Professor J. Tuzo Wilson, Dr J. Morgan proposed three years ago that the long linear chains of volcanoes seen in many parts of the world are the consequence of the motion of plates over hotspots in the mantle. The fundamental questions seem to be four in number. (1) Do hotspots exist—that is, are there regions beneath plates where temperature is anomalously high? (2) Do hotspots have a permanence during geological periods of time? (3) Are they connected to any deeper expression of convection such as a rising plume of material? (4) Do they have a global influence on plate motions, that is, is a knowledge of hotspot characteristics necessary to an understanding of the driving forces of plates?

The surface evidence that "something is going on" is indisputable from the long island chains. It was very difficult, however, to perceive any compelling evidence from the many contributions that would cause the last three questions to be answered in the affirmative. There seems as yet to be no clear agreement on the definition of a hotspot (Morgan proposed ten; at this meeting it was suggested there might be hundreds). Evidence from the geological and geochronological record contains too many contradictions to be regarded as supporting wholeheartedly a positive answer to question (2). Very little was presented that bore on questions (3) and (4), but good papers were given by Dr J.-G. Schilling (University of Rhode Island) on the rare-earth geochemistry of ridges and plumes and by Dr B. Minster (Caltech) on the kinematic evidence for plate motions and consequent inferences on hotspot stability. It is, however, difficult to avoid the conclusion that the hotspot hypothesis is indeed no more than that and is in need of some stiff theoretical support as the observational material is so equivocal.

A sparsely attended session was

devoted to the Earth Resources Technology Satellite. There can be more than one opinion of whether ERTS is yielding significant results but it was a disappointment that more did not come to learn for themselves whether ERTS has any uses for them. A particularly good technical introduction to ERTS was given by Dr S. Freden (NASA).

Perhaps the clearest impression with which one left the AGU meeting was one of vigorous controversy. There is disagreement about earthquake mechanisms, about plumes in the mantle, about the core-mantle boundary, about dilatancy in earthquake prediction and doubtless about all manner of other things.

METALLURGY

Superplastic Control

from a Correspondent

ONE topic of particular interest at present to physical metallurgists—grain boundary sliding—was the subject of a conference held at the University of Sheffield under the auspices of the Institute of Metallurgy on April 12. When a polycrystalline metal sample is deformed at relatively high temperatures, not only do the interiors of the individual crystals or grains deform (by well-understood mechanisms) to change shape consistent with the overall deformation but the grains also move bodily with respect to each other. The motion resembles the relative motion of peas channelled to pass through a funnel.

Dr D. McLean (National Physical Laboratory) opened the discussion at the conference by reviewing the evidence from elastic and anelastic damping measurements that grain boundary sliding results from motion of dislocations in the grain boundary in a manner similar to that in which lattice dislocations are responsible for plastic deformation of the grains. The situation is by no means clear cut, and different groups still have different concepts of the nature of dislocations in a grain boundary. This is surprising for, geometrically speaking, the position has been clearly defined by recent work of Dr W. Bollmann (Battelle Institute, Geneva). One indication of this lack of rigour in basic understanding is the proliferation of different nomenclatures for the differing concepts to accord with the various roles that the dislocations are expected to fulfil.

Some beautiful examples of dislocation arrangements in slid bicrystals of aluminium were shown by Dr C. A. P. Horton (Central Electricity Research Laboratories, Leatherhead). The electron microscope was again shown to be a vital metallurgical tool. It will surely lead to the definitive observations on the

structural aspects of grain boundaries as it has already done for dislocation structures within the grains.

Grain boundary sliding is of great practical relevance in that the ease or not with which it occurs, relative to other mechanisms of deformation, controls the ductility of materials at high temperature. It is also intimately associated with the phenomenon of superplasticity (the occurrence of extended deformation before fracture). The difference in the behaviour of some commercial and non-commercial materials was illustrated in a presentation of some results on a 316 stainless steel by Dr R. S. Gates (Central Electricity Research Laboratories, Leatherhead) which revealed many unexpected features.

There is still controversy about how the most meaningful measurement of grain boundary sliding is to be made. Some sliding that does not contribute directly to the extension of the material may undoubtedly occur, whereas other sliding gives an independent contribution to the extension. It is only just being realized that the two contributions are evident in extreme forms in superplasticity and low temperature creep behaviour. It was clear from the animated discussion led by Dr G. B. Gibbs (Central Electricity Research Laboratories, Berkeley) that much thought and many more experimental observations on both commercial and non-commercial materials are needed before even certain conceptual problems of the sliding geometries can be finally straightened out.

It was of undoubted interest to metallurgists to learn during the course of the meeting that grain boundary sliding occurs in ceramic materials even though a superplastic ceramic is still in the realms of conjecture. Detailed information was provided by Dr P. E. Evans (University of Manchester Institute of Science and Technology) on alumina, zirconia and scandia and by Dr R. T. Pascoe (Central Electricity Research Laboratories, Leatherhead) on haematite iron oxide. In the field of ceramics the concept of dislocations in boundaries will have to be modified as the common structures are no longer preponderantly cubic as they are in metals. Furthermore, there are difficulties in interpreting both the activation energy and the stress dependence of the observed strain rates in these materials in terms of accepted mechanisms of creep deformation.

Clearly there is much still to strive for in this field. As yet a complete understanding of grain boundary sliding is some time away and much further work is required before the sliding characteristics of grain boundaries can be predicted and the desired improvement made in material properties.



Poor Outlook for European Collaboration

THE pages which follow provide a vivid illustration of the richness of European science but very little evidence that the integration of Europe in the economic sense will be accompanied by the joint effort in research and development which circumstances require. The underlying trouble is that European governments, disillusioned as they have become in recent years by the conviction that public expenditure on research and development is uneconomic, have not been able to grasp the notion that the long-term economic and cultural health of Europe depends as much on a vigorous scientific community as on any other ingredient of the common enterprise. And although the summit conference in Paris in October instructed the European Commission to prepare a plan for the integration of European science before the end of 1973, it becomes increasingly clear that the commission's own ideas of what should be done are at once over-ambitious and needlessly neglectful of existing institutions. If the precedents of the past few years are an accurate guide, the chances are small that the commission will be able to meet the December deadline. This is a serious cause of anxiety.

The arguments for a closer integration of European science are elementary and compelling. In academic research, however defined, there is an urgent need to remove the sense of isolation that afflicts a great many of those who work in European universities and research institutes. The American experience since the Second World War has shown quite clearly that there are advantages of scale to be exploited by the scientific community, but these derive as much from the mobility of people and ideas as from the scale on which money is expended. It is an enormous source of benefit that people should be able to congregate in groups with common interests, either permanently in departments or institutes dedicated

to particular problems or in conferences and seminars. By comparison with the United States, Europe is not too badly endowed with active researchers, but people are much less free to move about. As time goes on, the way in which CERN has functioned as a focus of common activity in high energy physics emerges more and more clearly as an exception which proves the general rule that there are too few common European centres of intellectual activity in science. The European Molecular Biology Organization, it is true, may emerge as a similar institution, especially now that it will have a laboratory at Heidelberg to call its own, but that will take time. Organizations such as the European Space Research Organization, enmeshed as they have been in national rivalries and ambitious arguments for what is called a "European space policy", have conspicuously failed to function as common centres of intellectual enterprise. And it remains depressingly the case that in most fields of scientific work, European researchers are confined too narrowly to their universities and research institutions. The most conspicuous links between, say, immunologists

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in Holland or atmospheric physicists in Britain remain with the United States.

What the commission must recognize is that its first objective, so far as academic research is concerned, is to make arrangements for the greater mobility of people and ideas. To begin with, money is less necessary than the reorganization of national institutions—what the commission itself is fond of calling harmonization. Briefly, arrangements need to be made that will allow national universities and research institutes to employ Europeans from elsewhere within the community on equal terms. In the sense in which university researchers and teachers in France and Italy, for example, are civil servants, it is essential that in future other nations' citizens should become, if they wish, employees of the French and the Italian governments. In the long run, the best solution will entail some degree of disestablishment of the centrally controlled university system, but that is a hot potato. For the time being, the commission itself could usefully concentrate on some means by which the machinery of an equal employment policy could be created within the present framework. And it is not too soon for Dr Dahrendorf, the member of the commission responsible, to be asking how in the long run a framework should be laid for a European university system. Far better this than the commission's efforts, in the past few years, to define the rules for the transferability of professional qualifications from one country to another, now mercifully discredited by the simple argument that any such definition is bound to be at once needlessly restrictive and unfair to at least some members of the community.

The second need is that there should be some common European institution with money to spend on international conferences, seminars and travel on a European basis. In the past few years, national governments to their credit have been spending more generously in fields like this, but it has been left to national academies to handle what funds there are to spend, with the result that there has grown up a complicated system of bilateral agreements designed to ensure that each country can be confident that it derives as much benefit as it thinks it is entitled to. Valuable though this system has been, the time has now come when it should be abandoned and the best alternative is that the European Commission's own suggestion that there should be a European Science Foundation to administer funds like these should be implemented quickly. After all, if national governments are prepared, as seems likely, to contribute to a common fund for regional development, it is surely not unreasonable to ask that they should also make contributions to a much smaller fund to ease the movement of ideas and people from one place to another. It is entirely irrelevant that such a common fund would inevitably benefit the smaller European nations more immediately than the chief contributors. Indeed, if European collaboration means anything at all, it must surely follow that those most in need are most helped.

Another, more serious problem is the organization for spending money by way of grants on research projects of an academic character. By now, all the members of the European Community have well developed systems for spending money on research, but there are of course great variations from one country to another in the scale on which research money is made available. In Italy, for example, expenditure is by any standards low, while the

criteria by means of which decisions are made leave much to be desired. Politically, it is unthinkable that there should be a speedy amalgamation of the research councils and their equivalents on a European basis, but there is at least a case for working out, even at this early stage, a framework within which there can be a common procedure for financing European research. By all accounts, the British view is that the relationships between British science and scientific research in other European countries outside the European Community are so important that national institutions cannot at this stage be subsumed in European institutions, but this is a false position. There is no reason why the community as a whole should not be concerned to foster links with other European countries as the British government and the Royal Society are supposed to be. Other European governments, the government of France, for example, are supposed to have responded to the commission's proposal for a European Science Foundation much more negatively, insisting that national governments must remain responsible for financing national research more or less indefinitely. But that, of course, is an argument that must be met head on. If the European Community means anything at all, it means that there must be a deliberate pooling of European resources. So it is essential to make an early start on some machinery for dispensing research grants on a European basis and the commission's concept of a European Science Foundation, muddled as it is, would be a good beginning.

Is there any convincing reason why the commission should not insist on this part of its proposal as an essential ingredient of the package of proposals it has promised by December?

On industrial research, there is much more muddle to contend with. The commission has traditionally taken the view that the biggest prize to be won is in the more efficient exploitation of industrial research and development, and there is a long and not particularly successful record of endeavour in this field. The European Launcher Development Organization, which has now, not before time, abandoned its attempt to make an efficient satellite launcher out of the relics of the Blue Streak rocket, is a splendid illustration of the kinds of machinery which should be avoided in the years ahead. The proposals of the Aigrain working groups in 1968 for common enterprises in the development of such machines as advanced computers and telecommunications equipment, essentially devices for pooling development resources within similar kinds of organizations, have luckily not come to much. And there has been very little applause for the commission's own ambitious scheme, put forward by Mr Spinelli a year ago, that would have turned the commission into a kind of supranational government with large funds to spend on industrial development schemes of various kinds. The trouble is that there can be no logical basis for the central sponsorship of industrial development which lacks a common framework for industrial operations as a whole. This, after all, is a field in which the policies of national governments are inseparable from their interests that national industries should prosper. It is flying in the face not merely of unreasonable chauvinism but of reasonable self-interest that nations should willingly support common research and development programmes in the expectation that the outcome will be an enhancement of the common good.

EMBO

Another Step Forward for the Laboratory

Last week the reality of a European Molecular Biology Laboratory in Heidelberg came closer with the signing in Geneva of the agreement to establish it.

Now that the agreement to set up a European Molecular Biology Laboratory at Heidelberg is signed and sealed, molecular biologists can look forward to the emergence during the next five years or so of a centre which should have a place in Europe similar to that held by the famous Cold Spring Harbor Laboratory in the United States.

Early Days

The idea of a laboratory on a European scale was first put forward a little more than ten years ago at a meeting at CERN—that shining example of European cooperation in science—where the signature ceremony took place last week. Later, in 1964, the European Molecular Biology Organization (EMBO) came into existence with the object not only of founding a laboratory but also of financing fellowships and summer courses. To begin with EMBO received \$750,000 from the Volkswagen Foundation for a period of three years starting in 1966—the object was that the organization should prove itself and in the meantime seek more permanent support from European governments.

The first EMBO proposal for a laboratory (in 1968) envisaged something larger than the one that is now to be built. But the governments involved did not approve, to some extent at least because EMBO itself had not thought out in sufficient detail what the purposes of the laboratory were to be and what functions it was supposed to perform.

Then out of a meeting in Konstanz in 1969 came proposals that formed the basis of the plans for the laboratory that

have finally won acceptance from ten European governments. It is intended that part of the function of the laboratory shall be to provide a service to national institutes in, for example, the development of advanced instrumentation. It will also carry out advanced training and will, like Cold Spring Harbor, be a centre for meetings both formal and informal.

Heidelberg

The site provided by Germany for the laboratory is deep in the forest at Heidelberg next to the Max-Planck Institut für Kernphysik, which together with the Deutsches Krebsforschungszentrum has offered temporary office and laboratory accommodation so that scientific work can begin quite soon, before the laboratory proper is completed.

As far as staff is concerned, the total number of personnel is expected to reach 130 in 1976 and the full complement of about 300 in 1978. Of this number nearly sixty will be qualified scientists and engineers (QSEs), including about sixteen post-doctoral fellows, and there will be about 167 technicians, fifty-five administrative staff and thirty to thirty-five visiting scientists (at any one time).

There are also plans afoot for establishing an outstation of the laboratory at the electron synchrotron (DESY) in Hamburg and one at the high flux reactor in Grenoble. This will make possible experiments with intense X-ray and neutron beams.

Expenditure

Table 1 shows the expenditure envisaged in the years until the laboratory is fully operational. It includes an estimate of the way in which a special contribution to capital costs made by the German government may be spent. Ratification by the participating governments is unlikely to take less than a year, but during that time sufficient money will be available for architects to be engaged and other aspects of advanced planning to be completed.

Table 1 Global Costs of the Laboratory to Contributing Governments

Estimated ceiling of non-recurrent costs	1973 May– December Before ratification	1974 January– April	1974 May– December	1975	1976	1977	1978	1979	Totals
	After ratification								
Preliminary studies	71	63.5							134.5
Central laboratory			2,406	2,704	2,385	1,291	630	176	9,592
Outstation at DESY, Hamburg	568	140	213	77					998
Outstation at Grenoble	96	447	78	46					267
Total A	735	250.5	2,697	2,827	2,385	1,291	630	176	10,991.5
Possible application of German special contribution (DM 12,000,000)	537	113	1,100	950	579				3,279
Net non-recurrent costs B	198	137.5	1,597	1,877	1,806	1,291	630	176	7,712.5
Recurrent costs (estimated budget)									
Central laboratory			558	1,431	2,564	3,743			
Outstation at DESY, Hamburg	124	72	169	299	324	324			
Outstation at Grenoble	39	56	139	259	284	294			
Total recurrent costs C	163	128	866	1,989	3,172	4,361	5,066	5,595	
Global costs to governments (B + C)	361	265.5	2,463	3,866	4,978	5,652			

Costs are in thousands of accounting units at 1972 prices (1 AU = \$1.2).

SPACE

European Unanimity Still Hard to Find

by our Special Correspondent

The future of the European Space Research Organization is well defined but the remainder of Europe's space programmes are still in a state of flux.

EUROPE is scarcely more united over space than it has ever been. The veneer of unanimity achieved at last December's meeting of ministers in Brussels at which plans for a European Space Agency were tentatively formulated, has already been disrupted by the sudden end of the European Launcher Development Organization's work late last month and an outspoken attack on British attitudes to European space efforts by Mr Charbonnel, the French Minister for Industrial and Scientific Development.

In a statement issued recently in Paris, Mr Charbonnel declared that at the Brussels conference only the French and the Germans had any real contribution to make. Britain's suggestion—sponsored by Mr Michael Heseltine, British Minister for Aerospace and Shipping — that a "European NASA" should be formed was all very well, Mr Charbonnel said, but if Britain is not prepared to put more money into either L3S, the French launcher proposal, or the post-Apollo work, "they are scarcely in a position to ask us, in the immediate future, to push ahead with the project of a European NASA. If the English are not interested in anything — scarcely in the post-Apollo programme, not at all in the launcher, then in the name of what can they ask us to create an integrated organization?"

Such a firm statement does not augur well for the ministerial meeting planned for July, when the French intend to ask the other European countries to guarantee to purchase and use L3S when it is built.

Space Agency

The future of the European Space Agency will also have to be sorted out against the background of ELDO's effective demise. The original plan was to merge ELDO with the European Space Research Organization if possible by January 1974. But the ending of the ELDO programme following the withdrawal of finance by the French and Germans means that in practice all there is to merge at present is ESRO's programme, a French launcher proposal that at present is only a proposal, and the various projects that are currently being nurtured in national programmes — for example Britain's Geostationary Technology Satellite.

It is well known that the agency, which is unlikely to be formed in anything but name by January 1, will have to be based around ESRO. Over the past five years the structure of ESRO, with its comparatively powerful secretariat which is largely left alone to get on with the job once the decision to proceed with programmes has been taken by member states, has proved effective. If ESRO is to be part of the new agency, then this authority must be preserved, and Europe must not destroy its one successful space venture merely to create an organization with an impressive sounding name.

But it is difficult to see how the agency can emerge with a really strong management structure if such projects as L3S

are to be included. The French put forward L3S as an alternative to Europa III last year on the grounds that it would cost less and would be less risky. Mr Charbonnel has put the cost at about 2,400 million francs, and this figure is understood to include a 20% margin to allow for contingencies. The French proposal is that France will provide 60% of the finance and absorb any increases in the estimated cost of the rocket, providing that the rest of Europe, and in particular Germany, will contribute the remaining 40% of the finance.

But France is only prepared to do this if management control of the project lies in French hands. The French believe that the launcher can be built on time and at the estimated cost provided the management is strong. Yet at the same time, if the agency is created the French will doubtless want the launcher to have the stamp of European approval and cooperation, so that the agency is likely—if the French get their way—to have some sort of responsibility for the success of the project without having any real control over it. The agency might, for example, be expected to marshal the international finance for the project and keep an eye on progress so that it can report to the member states.

Similarly, Britain has offered its Geostationary Technology Satellite (GTS) as a collaborative project, but again control of the programme would be likely to lie within Britain which would provide most of the finance. This proposal by the British in fact clashes rather oddly with Mr Heseltine's insistence at the Brussels meeting that a strong European agency should be formed.

More Problems

Quite apart from these problems, there are enormous administrative problems involved in creating the agency. Integrating national programmes is one thing, but internationalizing national facilities and running expenditure is another. Countries with small national programmes are likely to have to increase their expenditure in order to pay for a share of the facilities that other countries already own, but which will be used for international programmes.

But if the structure of the new space agency is far from clear (and little progress has been made so far towards formulating it) at least ESRO's programmes within that structure are well defined.

Last month the organization chose two new scientific satellites, HELOS (Highly Eccentric Lunar Occultation Satellite) and ISEPS (International Sun-Earth Physics Programme) which will be launched in 1977 and 1979 (see *Nature*, 242, 547; 1973).

In the nearer future on the scientific front COS-B, a cosmic-ray satellite, and GEOS, which will study particle fluxes and electric and magnetic fields, are scheduled to be launched in 1975 and 1976 respectively.

ESRO's programme also includes studies on Spacelab (part of the United States shuttle programme). Six of ESRO's nine member countries are now participating in the project (Italy, Spain, West Germany, Belgium, the Netherlands and Britain) and Europe has to tell NASA by August 15 if it intends actually to build the laboratory for delivery to NASA in 1979. It is possible that France also will contribute 10% of the cost to the project if West Germany comes in on the French launcher proposal.

Plans for Spacelab

At present, three possible concepts of the laboratory are being studied including a general purpose laboratory and one of a modular construction that might prove more flexible. The laboratory will be carried into space in the cargo bay of the shuttle and will provide working facilities for up to four scientists. Although, in terms of cost, the laboratory is a comparatively small part of the shuttle programme—the cost of developing, building and delivering the first example was originally put at about \$275 million, while the cost of the shuttle itself will be thousands of millions of dollars—the laboratory is a key part of the programme.

Technically ESRO is fully committed to developing Spacelab, although the individual countries are not. There is, however, an escape clause, which states that if by August it seems as if the cost of the project will “unacceptably exceed” the original estimates, then Europe can withdraw from the programme. What “unacceptably exceeds” means has not been defined. But it seems more than likely that Europe will go ahead with the project, carried along by Germany’s enthusiasm.

Later this year ESRO is to appoint a scientific mission definition group to help decide what experiments should be flown in Spacelab when it is launched in 1979.

Applications Satellites

The third prong of ESRO’s current work, a particular growth area since 1971, is its applications satellites. Three programmes are currently underway. The European Communications Satellite programme provides for an orbital test satellite to be launched in 1976. At present competitive design studies are being made and a single contractor who will finalize the design and undertake development will be chosen by the end of the year.

The satellite will carry 5,000 telephone circuits and will be inserted into the European telecommunication system so that the telephone undertakings can see for themselves that it works. An operational satellite with a planned life of seven years should be launched in 1980.

The other applications programmes are Meteosat and Aerosat. Meteosat will take visible and infrared pictures of the Earth with a 40 cm telescope once every thirty minutes from a geostationary position over Africa. The satellite will play two roles—first, as an experimental satellite in the international Global Atmospheric Research Programme, and then as an operational tool in the World Weather Watch which is to follow the large research programme into weather formation that is planned for 1977.

Aerosat, at present the most controversial of ESRO’s applications satellites, is a joint programme with the United States with Australia and possibly Canada and Japan participating. ESRO is now selecting a United States industrial partner to co-finance the development of the satellites. Comsat, ITT, Fairchild, RCA Globcom and Western Union are the companies who have applied to join ESRO in the enterprise which will put two satellites into orbit over the Atlantic in 1977. The final choice of industrial partner should be made next month.

The project is an ambitious one intended to evaluate the possibilities of communicating with hundreds of aircraft at once and of running surveillance of them by satellite so that air traffic control over the oceans can become more precise.

Finally ESRO’s programme also includes paper studies of second generation applications satellites—a maritime satellite (MARSAT) to assist navigation, an Earth resources satellite, and a television broadcasting satellite. All these are at a very early stage where ESRO is talking to the potential users of the systems in a process of mutual education in which ESRO learns what is wanted while the users learn what can be done, MARSAT is the most prominent of these programmes, as Britain’s GTS is also a maritime satellite, and Britain’s offer

of it as a cooperative project has led to a comparison of the two satellites by ESRO. The results of this study should be available shortly, and it is by no means certain that GTS—which is essentially a technology satellite—will prove a suitable base on which to build an operational satellite.

Increasing Confidence

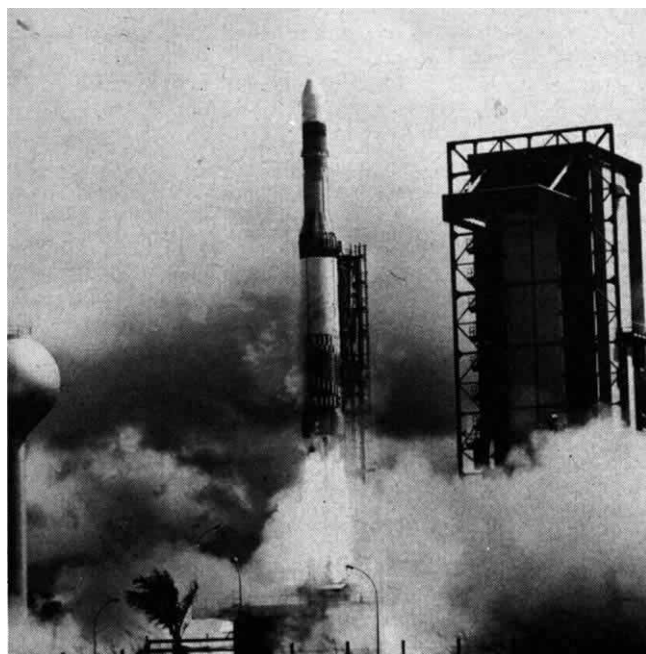
This extremely solid position has grown from the uncertain days of 1970 when expenditure was less than half what it is today, and when France and Denmark were considering withdrawing from the organization because the member countries could not agree on an overall programme.

ESRO’s past record is impressive. Since 1964 seven scientific satellites have been launched, of which five have been completely successful. ESRO-1b, launched in 1969, was something of a disappointment, although it did collect some valuable data, and TD-1A, Europe’s largest and most expensive satellite so far, suffered badly from the failure of its two tape recorders. Nevertheless faced with the problem of collecting data in real time, ESRO has put together enough tracking stations round the world to collect about 80% of the data from TD-1A.

Of the seven satellites, the last six have all been delivered on time to NASA for launch, and since 1967, when the cost estimates for TD-1 and TD-2 went off beam, ESRO has built all its satellites to cost. The willingness with which NASA is prepared to cooperate with ESRO on the post-Apollo studies, and the way in which five United States industrial companies are competing to put their money into a joint programme with ESRO on Aerosat, is a mark of ESRO’s standing outside Europe.

Downhill

The repeated failures of ELDO, however, are quite another story. Founded in 1964 following pressure from Mr Peter Thorneycroft, then Britain’s Minister for Aviation, who wanted a continued use for Blue Streak, the original estimates for the development of a launcher was about \$195 million to be spent over five years. In the event, ELDO has spent \$720 million over nine years, all to no effect. Eleven launches have resulted in five successes (the first five launches) and six more or less disastrous failures. Britain’s Blue Streak functioned perfectly each time—the first launches were either Blue Streak alone or Blue Streak with dummy top stages—



First and last launch of Europa II.

but repeated failures in stage separation and ignition of upper stages coupled with rising costs gradually sapped confidence and Britain's decision to withdraw in 1968 was in many ways the beginning of the end for ELDO.

The mistakes made in forming ELDO and running it are well known. The attempt to strap together assorted bits of European rocketry to make one powerful launcher was at best ill-advised, but much more damaging was the attitude of the member states that formed ELDO. The organization was set up in such a way that it had little control over the activities of the companies that built the rockets, and the way

in which the programme was endlessly strung out was guaranteed to breed political crises. Several failures in a short length of time would have been far less damaging and far more acceptable.

The failure of ELDO undeniably lies with the member states rather than the organization's secretariat. Where Europe has had the courage of its convictions—in providing ESRO with a strong structure—it has had valuable returns for its money, and if the new agency is to succeed then it too must be given the freedom it needs to carry out programmes, and must not just be given a coordinating role.

EUROPEAN ECONOMIC COMMUNITY

Science Policy in the Balance

by our Special Correspondent

The past few months have been a critical time for science policy within the Community. Commissioner Spinelli's policy for science has not found favour with the European countries and a reappraisal of science policy is currently being carried out. In this article the difficulties surrounding the making of a science policy for the Community are analysed.

COMMISSIONER ALTIERO SPINELLI'S carefully constructed plan for a common policy for scientific research and technical development within the European Economic Community lies in shreds after being considered by a special committee set up by the permanent representatives of the European countries in Brussels.

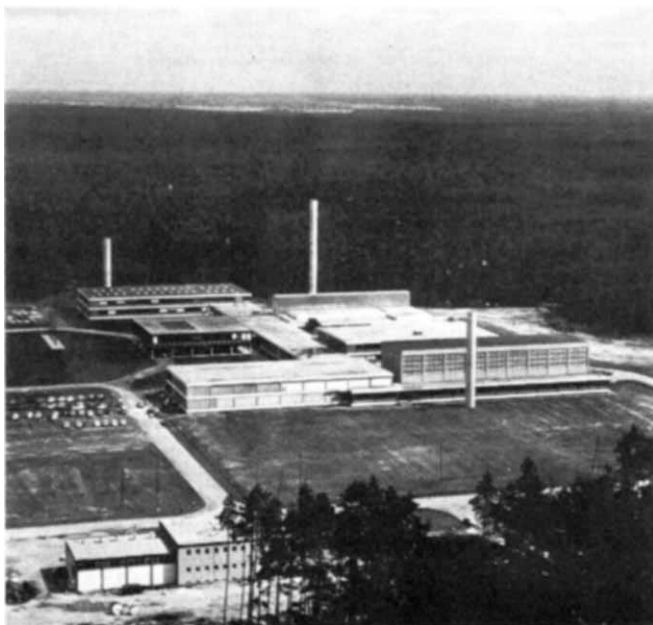
This setback places the Commission in the embarrassing position of having to produce an acceptable science policy by January 1, 1974, as ordained in the summit meeting at Paris in October 1972. At best this will be a race against time now that a completely new outlook on science within the community is necessary, and at worst the community will have to make do without a science policy until well into 1974.

But what has caused the downfall of the Spinelli document which was launched with such enthusiasm? In June 1972, Mr Christopher Layton, at that time Spinelli's chef de cabinet, came to London to publicise the contents of the document, but it seems that within the British Government, in particular, the document was met with indifference. From all accounts the French also objected to parts of the policy document, and with some support from other countries the British and the French between them have succeeded in completely deadlocking the Recherche Scientifique et Technique Committee set up by the Council of Ministers which has been examining the report. On May 8 the science ministers of the Community were supposed to meet in Brussels to discuss the Spinelli document but when it became clear that no agreement could be reached the meeting was postponed.

In essence, the difficulty with the Spinelli document is that it calls for the individual nations to lose too much

of their autonomy too soon. As an example the third resolution of the plan called for "the Community to be informed of all plans and programmes which involve financial aid from public funds and because of their scale or type may be of Community interest, and to these ends take all necessary steps to lay down the criteria for this information and ensure that it is received in time". Clearly this was too much even for a country newly committed to Europe to swallow.

But another serious difficulty with this plan, which has been highlighted in recent months, concerns the call for a European Science Foundation to be set up. On this particular issue the feeling among delegates in Brussels and scientists in Europe has been that such a foundation, if set up, should not be restricted to countries within the Community and that other European countries should be invited to become members. Meetings have been held, first at the Royal Society in Britain last December and more recently in Munich by representatives of research councils and



The Joint Research Centre's establishment at Karlsruhe. The chief activity at the centre is the study of plutonium-containing nuclear fuels.

academies of Europe to determine whether or not a common feeling exists for the setting up of such a foundation. A further meeting will be held in Paris in September at which it is likely that some resolution will emerge favouring a Europe-wide science foundation.

So even if detailed agreement with the Spinelli document has not been obtained among the representatives of the nine member states it is likely that the scientific community within Europe will take matters into its own hands and produce a proposition which the Commission will be asked to support.

Another item in the Spinelli plan, which has come to fruition in the past few months, is the recommendation that an advisory body be set up akin to the Advisory Board of the Research Councils in Britain, composed of independent and non-official representatives, who would be charged with advising the Commission on research and development matters. This committee, called the European Committee on Research and Development (CERD), has now met once under the chairmanship of Professor Casimir of the Netherlands. Mr Spinelli also recommended that the Commission should have a full-time science adviser appointed on a two-year renewable contract who would also act as chairman of CERD. As yet no decision has been taken to appoint such a person.

But in spite of the implementation of these specific parts of the proposed common policy on science and technology the chief part of the document lies dormant. So how is the Commission going to be able to produce an acceptable science policy by the end of the year? As luck has it, responsibility for science and technology within the Commission now rests with the German, Professor R. Dahrendorf. Professor Dahrendorf is taking a completely different line towards science policy, at least for the time being, to that taken by his predecessor. The new policy which is at present being drafted, and is unlikely to see the light of day outside Brussels until well into the autumn is, from all accounts, being framed in terms of specific projects for international collaboration rather than being based on broad philosophy as was the Spinelli document. Clearly such a document is much less likely to run into trouble with the science ministers, and if the collaborative projects are chosen sufficiently carefully then what will pass for a science policy will become accepted by the member states not unduly late next year.

In the light of the experience of the past few months the policy document prepared by Commissioner Spinelli and his advisors has been shown to be premature. Without doubt, a more cautious and conservative approach is needed when drawing up Community-wide policy statements, at least at this stage in the development of the Community.

The past few months have seen the emergence of CERD from being a dream of Spinelli's to being a reality. But the question which is being asked in Brussels and elsewhere is what will be the relationship of this body to the COST and PREST groups. PREST is a committee set up in 1965 by the Community's Medium Term Economic Policy Committee as a committee on scientific and technical research policy to "study problems which would be posed by the formulation of a coordinated or common policy for scientific and technical research and to propose measures to enable such a policy to be put in hand bearing in mind such possibilities as may exist for cooperation with other countries". When it became clear that such international programmes within Europe needed the cooperation of countries outside the then community of six countries COST was set up to include 19 countries—all the European non-communist countries. The work of COST was highlighted in last year's European supplement of *Nature* (237, 202; 1972).

But is there a need for both PREST and CERD, and if there is, what is the relationship between the two? First, CERD is composed of individual experts to advise the Commission while PREST is a body composed of official repre-

sentatives from the respective countries which therefore is more closely allied to the Council of Ministers. But it is indeed possible that some conflict could arise between the two bodies.

As an example it seems likely that when Professor Dahrendorf has drafted his new science policy for the community he will ask CERD to comment on it. It will then be passed on to the Council of Ministers, which could either set up a special committee to study the document, as it did for the Spinelli policy document, or it could call upon the PREST group consisting now of representatives of the nine member countries to study the document. The feeling in Brussels is that the Council will adopt this latter course for the simple reason that the Dahrendorf policy document is expected to contain several recommendations for international research projects which is just the field of interest of PREST. Clearly the document will not be passed on to the Council until CERD approves of it. But what if PREST takes exception to the document or to parts of it? Such a situation will lead inevitably to an unhealthy conflict, the mere thought of which causes cold shivers to be evident in the Commission building in Brussels.

But is there a solution to all this? At present there is no link between CERD and the PREST and COST groups, but it would not be a surprise to some people if the science adviser to the Commission—if he survives the Dahrendorf redrafting of the policy—will turn out to be someone who is also intimately connected with PREST and COST.

This past year has seen a revival of the fortunes of the Joint Research Centre of the European Community. For the first time since 1968 the four laboratories of the centre have a four-year budget to be compared with the one-year contracts on which they have been operating in recent years.

The four-year budget, which was agreed on February 6 this year, is for 180 million units of account (one unit of account was one dollar before the recent devaluation). This will provide employment for 1,700 scientists and support staff.

Most of this—157.2 million units—will be spent at the Joint Research Centre which will employ 1,440 personnel.

Table 1 Projects to be Carried Out by the Joint Research Centre

	Appropriation (million units of account)		People employed
	1973	Four years	
(a) Nuclear projects			
Waste treatment and storage	1.57	6.90	75
Plutonium and transplutonium elements *	4.95	{ 13.00 8.65	210
Materials science	1.94	8.50	89
Reactor safety	4.83	21.10	232
Applied data-processing	1.38	6.05	51
Information analysis bureaux	1.16	5.10	51
Central Bureau for Nuclear Measurements (CBNM)	4.45	20.35	170
Technical back-up for nuclear power plant operators	1.40	6.10	60
Training	0.33	1.45	15
Surveillance/management of nuclear materials †	1.23	5.40	57
Contract research	0.42	1.85	17
Management and coordination	1.80	8.10	79
(b) Non-nuclear projects			
Standards and reference substances	1.24	5.40	62
Environmental protection	2.97	13.00	142
Remote sensing of Earth resources	0.24	1.05	10
(c) Petten high-flux reactor ‡	5.26	23.00	95
(d) Use of Ispra-1 reactor	0.50	2.20	25

* Supplementary programme involving all countries except Italy.

† Supplementary programme involving all countries except France.

‡ Supplementary programme involving Germany, Belgium and the Netherlands.

Although the research programme is for four years it will be reviewed in two years' time. The detailed programme is shown in Table 1.

Since the ministers agreed on the programme of research outlined in Table 1 a further 20 million units of account have been allocated to the Joint Research Centre to be spent over the next four years. The chief item of this list is a sum approaching 2 million units of account to be spent on producing hydrogen by nuclear power.

But one of the most cheerful notes to be sounded about the community's research plans in the past year is the renewed interest in the possibility of obtaining power from a controlled fusion reactor. Between 1972 and 1976 the Commission will spend 56,196 million units of account on fusion research, all of it on contract to laboratories within the enlarged community. This sum represents only about 30 per cent of the total being spent on fusion research, that being the percentage aid granted by the Community.

But there is great enthusiasm in Brussels about the Community's fusion programme. There is a feeling that here, at last, is a programme that will achieve all that Euratom set out to do when it was set up in 1957 but in the field of nuclear fission. The nuclear fission and reactor part of the Euratom programme ceased to be viable at a very early stage when no agreement could be reached on what type of reactor to develop in the Community. The vital question

was whether the Community should concentrate its efforts on gas cooled or water cooled reactors. The unfortunate fact at the time was that each individual country had developed its own research to such a stage when Euratom was set up that it was embarrassing for them to have to sacrifice so much knowledge to contribute to a Community programme. The same will not happen in fusion, it is argued, for the research is still at an early enough stage and the expense of the research is such that no single country within Europe can support research in all aspects of nuclear fusion. It can only be hoped that the cautious optimism which surrounds the fusion research programme will prove to be well founded.

What is the long term future of the Joint Research Centre? No longer are these laboratories solely geared to nuclear projects as can be seen from Table 1. The question is whether Commissioner Dahrendorf will include some comment about the future of the Joint Research Centre in his policy document. Little contract research is done at these establishments at present. But maybe this is where the future should lie. The Harwell establishment of the United Kingdom Atomic Energy Authority has proved its worth in recent years by going more and more into contract research and in fact earning a great deal of money to offset against its budget. Perhaps the Commission should be thinking along such lines for its own laboratories.

COMPUTERS

Need for Collaboration in Europe

M. ALLEGRE

120 Rue Cherche du Midi, Paris

Computing points the way which must be followed by other industries before true European collaboration can be realized. Mr Maurice Allegre, who has been closely involved with France's "Plan Calcul" indicates in this article the way in which a new progressive change in attitude can lead to the effectiveness necessary in such a competitive sphere.

THE young computing industry is original in many respects. Within twenty years, computing has become one of the major world industries, having a large effect on daily life. Further, the leading computer country is undoubtedly the United States, and its example is unrivalled in the economic history of the world.

After two years of uncertainty, this industry has just begun to move forward again, admittedly at a somewhat more sober pace than before, but nevertheless sufficiently rapidly to guarantee a rosy future. For many years, IBM, with more than 50% of the world market, has held the record for capital investment; projecting current trends one might easily predict that, by 1985, IBM could also become the top company in the world as regards turnover, even overtaking General Motors. In the United States, however, as in the

rest of the world, certain reactions are setting in which might modify this prediction.

Situation in United States

First, the government in the United States is seriously concerned about the disadvantages of this dominant position. Moreover, these doubts are not new, because with the exceptions of the United Kingdom and Japan, where long-standing protectionist policy towards national industries exists, it is in the United States that the role of IBM in equipping government departments has been most severely reduced. Today, the action of the United States government has become more incisive; after several minor skirmishes in the past, the whole weight of the antitrust laws is now in force and, for the first time, the openly affirmed intention is nothing less than to "dismantle" the computer giant completely. The existing world organization of IBM, however, makes this plan somewhat difficult to put into operation. Certain more limited steps, such as the obligation to publish well in advance and in great detail any departures from normal techniques will, however, allow the more serious effects of this domination to be avoided. This is a real danger, as IBM seems to have understood from the way in which it has just compensated Control Data in an out of court settlement of an antitrust case.

The IBM case will perhaps one day be as famous as the Standard Oil case, Standard Oil, of course, was divided on a regional basis, because of its monopolistic domination of the market—the classic example of antitrust legislation at work—giving birth to such offspring as Standard Oil

(Ohio); in the same way, IBM might be divided, with IBM (Europe) forced to become a separate entity. Another possibility, however, is division by conduct, a prospect which is perhaps even less appealing to IBM than regional dismemberment. One thing is certain: among IBM's American competitors, the list of failures has not ended with General Electric and RCA and the sole hope of survival in face of the renewed aggression of IBM lies in the antitrust action of the United States government.

Relevance to Europe

Things are also beginning to happen outside the United States. Foreign domination in such an important field has within the past decade led to reactions most aptly termed as "economic nationalism". Though humble in origin, these seeds are today beginning to bear fruit, and they will have a considerable effect on the international scene. More than six years ago, France launched the "Plan Calcul" for reasons which have been justified by the passage of time. Germany quickly followed suit, and Britain has for a long time shown a great deal of concern for its own computing industry. Japan has long since been past master of the art of simultaneously promoting and protecting a national industry and has created a computer industry on a large scale, and other countries, notably in Europe, are today on the threshold of similar projects. At this point one must also stress the great efforts being made in Eastern Europe, where the Soviet Union and other countries have generally been sharing out the tasks, undertaking to produce a range of compatible computers. I have recently returned from Moscow where I had the privilege of being present at a general presentation of these machines. The technique is not yet very elaborate; but its existence is proof of the depth and continuity of the effort made by these countries, for the same reasons as the Western world.

The Future

During the next few years, Europe will play an increasingly important role in the competition which has only just got under way. With a more rapid growth rate than the United States, Europe should, by the end of the present decade, have something like 30% of the world market, while the United States will have barely 50%. This illustrates the importance of the advance on the old Europe, which at present has only some 25% of the market.

Europe has for some time been aware of the problem in the computing industry. For example, since 1968, I have been president of a specialist computing group in Brussels within PREST with responsibility for putting forward a "harmonization" of scientific and technological policies among member states of the European Community, and I have come up with an interesting observation. All the members spontaneously agreed that computing was first and foremost an industrial matter and that one has to make the distinction between European branches of organizations whose decision-making bodies lie outside the European Community and community-based companies. A common problem is that of the necessity for the development of a truly European industry. Undoubtedly the idea of a powerful computer produced in common by all the European manufacturers came too soon. Nevertheless, the ideas have been planted and will be brought to fruition sooner or later in one form or another—they are already in the process of being realized. A report at present in preparation by the European Commission will soon give them official blessing.

Three European countries have already taken the decision to help the development of their national industries. But although their intervention may seem unusual, it is intended to redress the balance of opportunities and to make possible

competition which would otherwise have been futile. The facts bear out this attitude, just as heavy international competition today forces the pooling of individual effort. Aware of the "economies of scale," European governments now encourage their industries to merge. Since the launching of the "Plan Calcul", France has stressed that this does not mean a simple operation at national level. On the contrary, it means the implementation of a programme in two stages which can be summed up thus: "Exister d'abord, coopérer ensuite".

Already many links have been forged between advisory and service bodies in French computing, where this sector is highly developed, and English software manufacturers. Recently in a sector which might be termed computer peripherals, and which regroups the manufacturers of mini-computers, terminals and peripheral equipment, an agreement has just been signed between a French and a German mini-computer manufacturer. The movement towards restructuring is only just beginning to develop in Europe. But the computing industry is above all about computing systems. It is better to use that expression than that of computer manufacturers which is today far too narrow. Having given proof of its existence by putting on the market an original range of medium and large computers, the Societe Francaise Compagnie Internationale pour l'Informatique (CII) has for the past two years been able to move on to the second stage of the programme cooperation. After many months of discussion, no agreement was reached with ICL because the British seemed more than anything to want to retain certain technical peculiarities—it is not easy to construct a common car when, completely against common practice, one partner wants to put the driving wheel on the right-hand side. On the other hand, the withdrawal of RCA allowed Siemens, which had taken over RCA's licence, to sign a general agreement with CII in February 1972 as a result of which the two firms decided to share all the tasks of planning, manufacturing and marketing computing systems. The Dutch firm Philips is at an advanced stage of negotiation to join the other two companies, and the past year has seen a new task, as yet unnoticed, get under way—that of the precise definition and identification of the future CII and Siemens range. Further, since January 1, 1973, the Siemens group in France has been totally integrated into CII and a reciprocal agreement operates for CII in Germany.

With a remarkable spirit of independence, the German firm Nixdorf is for its part trying to resolve its own dilemma: to get out of the tight computing stranglehold, in which it has succeeded so well until now, and so come to some necessary international arrangements. One may well fear an eventual Nixdorf-ICL agreement which would ultimately lessen the chances of a more general but nevertheless more desirable regrouping with Europe.

As for ICL, will it be able to resist certain temptations from the other side of the Atlantic? The United Kingdom government seems to be heavily orienting its national protegee into international cooperation, primarily in Europe. Perhaps it would be advisable to start with an agreement on certain peripheral matters. In any case, in the long run there will only be room for one large truly European computing organization, and the way in which ICL will eventually come to join the already formed continental nucleus will perhaps become clear in due course. The three ministers concerned in France, Germany and the United Kingdom clearly expressed their wishes in this direction to their national companies at the end of last year.

Finally, as they awaken to the computing possibilities, other European countries should come to join the multinational body now being constituted. When it has been sufficiently organized, this body, backed by a large share of the European market, can think about opening up the American market, for example by a balanced cooperation

with one of the small fry remaining on the other side of the Atlantic. Until such time, any cooperation with an American company can only result in imbalance in favour of one or other of the partners. It is certainly unthinkable that the European companies and governments should even unobtrusively abandon their many past efforts. On the other hand, a more rapid development in the American situation could create favourable opportunities for European firms. They must not come too soon, however, if we are to be able to take full advantage of them. One last point is worth mentioning: in Eastern Europe as in the West, the process of unification is in progress and the same causes—the necessity for a computing industry, and the desirability of a joint approach—are having the same affects. Will these two European industries remain forever on parallel tracks? Without envisaging events which cannot happen because of economic and political differences, it is nevertheless probable that certain points in common should be found in the respective interests of the two parties.

Having thus gained a right to exist through a minor share of the market by sheer strength and active government aid, the European computing industry is beginning to increase its capacity for future competition by creating a truly multinational unit, that is a unit in which there is no decision-making body with superior powers to any other. In order for a united Europe to exist, there must first of all be collaboration on an industrial level. To achieve this, European manufacturers are committed to achieving a new method of cooperation which will give real meaning to the concept of multinationalism. The risk is considerable but it is worth taking. In this sphere, computing seems destined to set an example in the difficult path it has embarked on.

Faith in the importance of the task and in the necessity for it to succeed breeds the desire to innovate and seek new formulae. From these will come a new progressive change in attitude which alone can result in effectiveness which is vital in such a highly competitive sphere.

IRELAND

New Moves in Irish Science

C. Ó hEOCHA

University College, Galway

The chairman of the Irish National Science Council describes the organization of research and development in a small country with a modest science budget.

Boyle, Kirwan, Higgins, MacNeven, Rowan Hamilton, Kane, Stokes, Tyndall, Fitzgerald: a formidable, but partial, list of great Irish-born scientists¹. Technologists and inventors could be added, such as Muspratt, Holland and Parsons, as could Bernal, a pioneer of the concept of science policy. In the words of an editorial in the *Endeavour* on Irish scientists "the quality of their work is noteworthy for so small a country and deserves wider appreciation"^{1,2}. Science in Ireland has for long been fostered by the Royal Dublin Society (established in 1731) and the Royal Irish Academy (1785), and schools of science, engineering and medicine have long histories in the university colleges. Nevertheless, conditions in Ireland were such that many of its most distinguished scientists performed their work outside the country.

A little over fifty years ago, twenty-six counties of Ireland gained political independence and successive native governments have assisted industrialization. But political problems, both internal and external to the country, caused emphasis to be placed for many years on industries catering for the home market. When national economic and social planning was introduced about fifteen years ago, it helped to bring about a period of sustained economic growth, and the industrial and service sectors, in particular, expanded and export trade developed greatly.

Since independence, scientists and others have worked to build up indigenous science and technology of international standard, and since the late 1950s the scale of scientific activity

has developed rapidly, particularly in disciplines related to agriculture. Thus, when the British Association for the Advancement of Science met in Dublin in 1957, a listing of scientific institutions did not contain An Foras Talúntais (The Agricultural Institute)³. This institute was, in fact, established in the following year under the dynamic directorship of Dr Tom Walsh, and it is a measure of his success that by 1967 it accounted for 59% of expenditure on research and development within the government sector. Facilities for education and technical training were also improved during this period—universities expanded and new technical colleges were established. Economic growth was given an impetus by the creation in 1966 of the Anglo-Irish Free Trade Area and, most importantly, by the adherence of Ireland to the European Economic Community in January of this year. Membership of the community, however, creates problems as well as opportunities for a small country such as Ireland. The improved contact with neighbouring countries will be stimulating, but membership highlights the need to concentrate in our scientific as well as other activities on those areas which give the country comparative advantages.

Resources

Resources are, of course, limited—the population is only 3 million and it is unbalanced in that there is a preponderance of young and old people as a result of sustained and heavy emigration, which fortunately has slowed down in recent years. On the basis of gross national product (GNP) per head, Ireland is the least developed member of the EEC⁴. Expenditure per head on research and development, and the ratio of gross expenditure on research and development (GERD) to GNP are also lower than in the other member countries. On the other hand, if the number of papers published is any criterion, the productivity of Irish scientists is high. Thus, when the

number of published papers listed in the five editions of *Current Contents* in 1971 is related to the populations of the countries of their origin, Ireland is seen to be on a par with Austria, Belgium and Finland, and not far behind the Netherlands, France and Norway. As pointed out at a FEBS meeting in Dublin last month by Dr A. H. Hughes, however, "while publication is the measure of academic progress, in the brutal world of business the better your work the less likely it is to be published". Man does not live on science alone, no matter how acceptable to international journals.

That there are structural weaknesses in the science system in Ireland is apparent from the research and development statistics^{5,6} (figures for the science budget as a whole are not yet available in the detail needed to base the analysis on them). The total manpower involved in research and development in 1969 was 3,850, of whom 1,550 were graduates and 1,000 technicians. The overall expenditure on research and development is low (£14.3 million, or 0.74% of GNP, in 1971, of which the government supplied 60%); it is expended in the following sectors: government, 43.4%; business enterprise, 39.7%; higher education, 14.2%; private non-profit, 2.7%. Most of the expenditure is aimed at improving the country's economic capability, with considerably lesser sums being devoted to community services and the advancement of science; there is no expenditure on defence research and development. Between 1967 and 1971 support for research and development has grown at a rate of more than 12% a year in real terms.

Government Sector

Within the government sector there are only a small number of bodies concerned with research and development, but they use a very high proportion of research funds from public sources. Although the absence of a multiplicity of institutes is fortunate, the failure by other sectors, notably industry, to develop the capability to attract public funds, particularly for experimental development, implies a weakness which contrasts with the situation in many developed countries. Industry in Ireland consists largely of small firms having limited scientific expertise and thus having difficulty in assimilating relevant technical information, let alone performing research or development. There are, however, recent signs of improvement; for example, expenditure on research and development in the business enterprise sector has been rising steadily, even though such expenditure is small in relation to industrial output and is mostly confined to a very limited number of firms. The industries which devote most funds to research and development have not changed appreciably for some years: the food and drink group is by far the largest spender, followed by the electrical and electronic, utilities, and chemicals and drugs groups. Expenditure on research and development in science-intensive industries is still low and has not kept pace with the growth in exports from these industries; this is a reflexion of the growth of investment from abroad in export-oriented science-intensive industries⁷. To date such Irish-based subsidiaries have established few research and development facilities in the country. Efforts to attract such facilities are being intensified and a research park at Naas, sponsored by the Industrial Development Authority, has had some success. The encouragement of technological innovation in firms committed to grow in Ireland is being encouraged, with skill-intensive industries particularly favoured.

These considerations highlight the important role of the government-supported Institute for Industrial Research and Standards, which accounts for most government research and development funds for industrial research (about 16% of the 1971 total and 14.2% of that in 1969).

In fact, government expenditure on science has been largely concentrated on agriculture and related activities, which

account for about two-thirds of public expenditure on research and development and three-quarters of the expenditure on scientific and technical information (STI) services. Thus, 35% of Ireland's total research and development, including the contribution by industry, is devoted to agriculture, reflecting the country's traditional dependence on farming. Research oriented toward increasing farm production has been predominant in the past, but food science and technology are now receiving special attention, with increasing emphasis on market research.

Expenditure on research and development in institutions of higher education has remained static for many years at 12–15% of the national total, percentages which are comparatively small by international standards. Only about 1.5% of total funds for research and development were devoted in 1971 to marine resources, this in spite of the extent and potential of the Irish coastline and continental shelf. Research and exploration in the marine environment is expensive and the involvement of EEC funds in this endeavour may be necessary if Ireland is to benefit fully from its situation in the Eastern Atlantic. The establishment, for example, of a European centre for marine science in Ireland would be a most welcome development. Ireland has also been late in discovering its mineral wealth and in realizing the need to invest heavily in scientific activities related to their exploration and exploitation.

Government expenditure on scientific activities, including research and development, is a matter for departments and the operational bodies within their sector. Thus, the vote of the Minister for Agriculture contains grants-in-aid for An Foras Talúntais, as well as a substantial sum for research within his own department; the Minister for Industry and Commerce provides in his vote for the Institute for Industrial Research and Standards while the Minister for Local Government's vote contains funds for An Foras Forbartha (The National Institute for Physical Planning and Construction Research). The Minister for Finance has sought the views of the NSC on the long-term programmes of some of the research institutes and this procedure has led to some reorientation and concentration of effort.

The bulk of the finance for university institutions is allocated by the Higher Education Authority (HEA), a newly established statutory body charged with coordination of expenditure on higher education. The authority is provided for in the vote of the Minister for Education. The National Science Council (NSC), provided for in the vote of the Minister for Finance, supports research projects of high scientific merit as attested to by referees, many of whom are abroad. Projects having economic and/or social potential, as well as scientific merit, are particularly encouraged. A bridging committee of the NSC and HEA has been formed to coordinate matters of common concern.

National Science Council

In December 1967 the government, following receipt of the joint Irish/OECD Report, *Science and Irish Economic Development*⁸, established the National Science Council to advise it on matters of science policy. Members of the council are drawn from business, higher education and the public service; it reports to the Minister for Finance, who has responsibility for long-term economic development policy. The Minister stated at the inaugural meeting of the council that "... while all science is your concern, your attention as a council must be focused, at least for some time to come, on those aspects of science and technology which foster economic progress".

The council has undertaken the following activities, among others: publishing studies as a basis for science policy formulation and the selection of priority areas; interacting with and reviewing the medium and long-term programmes of the state-supported research institutes and other scientific bodies;

establishing a research grants scheme for universities and other institutions of higher education; formulating a scheme for research and development support to industry, which is administered by the Industrial Development Authority; communicating with scientific bodies in other countries and with appropriate international organizations with a view to bringing about greater Irish involvement in joint scientific projects.

As its four-year term of office drew to a close, the council after an evaluation of its own role, saw a need for change and made recommendations to the government concerning the powers and functions of a new body to succeed it⁹. The NSC was concerned that this body could ensure that technical programmes arrived at within the vertical departmental structure of government would be capable of dealing with the many horizontal problems, cutting across traditional departmental responsibilities, which face society today. It was also concerned that short-term financing of scientific programmes would be consistent with long-term policy for the attainment of national goals, while at the same time stimulating the creative drive of working scientists and of entrepreneurs in technology-based industry. The government accepted the advice that there should be established a statutory body with wider powers than those possessed by the present council, but postponed a decision on the detailed mechanism for implementing this decision. Meanwhile, the members of the first National Science Council were invited to continue in office.

OECD Review

Earlier the government, on the advice of the council, invited OECD to review Irish science policy, as well as policy for scientific and technical information. These two reviews were closely coupled as they proceeded in parallel; two separate "confrontation" meetings were held in Dublin in March of this year and full reports will be published by OECD in due course.

The country's overall economic and social policy formed a framework for the reviews. This calls particularly for the provision of industrial employment at an increased rate, as manpower employed in farm production continues to decline. In the long term, the examiners saw the much-needed increase in funds for research and development coming from the business enterprise sector, but in the meantime, and particularly as part of the strategy of preparing for full integration into EEC, they urged the government to consider increasing the level of its support for research and development, particularly that performed within manufacturing industry. They recommended that a state-sponsored advisory service be established to provide technological, management, financial and other relevant information for small and medium-sized firms.

The examiners see the higher education sector as having a crucial role in relation to the education of qualified manpower; it is here that they see the main potential for growth within the science system in Ireland. The achievement of this growth will, however, require energetic and skilful guidance from the resource allocating bodies, as well as the evolution of research policies within institutions of higher education.

The examiners found that Ireland, in common with many other countries, has neither a centralized science policy nor a coordinated policy for STI. They say that much of the difficulty arises from the limitation of the NSC role to a strictly advisory one, leaving it without effective powers of coordination.

The examiners agree that there is a need for a new statutory body to succeed the NSC and recommend the title National Board for Science and Technology (NBST). Its purpose would be to draw up and coordinate a central science policy. They commend recent approaches to detailed programming by the

state-supported research institutes; in this way the information needed to make choices in future between different priorities and solutions in applied research and development will become available. The examiners emphasize the need to relate applied research and development closely to industrial and agricultural production and to relevant marketing intelligence.

Role of National Board

The NBST would formulate, under the direction of the Minister for Finance, a central science policy, and would prepare an overall science budget which would be presented to a Committee of the Cabinet for Science and Technology, but government departments would continue to have financial and other responsibilities for scientific institutes under their aegis. The NBST would have a special fund with which it would promote the filling of gaps in the national scientific effort. It would, through its influence on the science budget, including an STI sub-budget, achieve coordination and concentration of scientific activities, within the scientific community the establishment of focal centres or "centres of excellence" is widely acknowledged as desirable, but the implementation of such a policy is at present difficult, not least because of the uncoordinated funding of science and technology by government departments. The report envisages that a number of committees would report to the NBST; the STI examiners specify two such committees, one concerned with the coordination within the library network of documentation acquisition, storage and retrieval policies, the other with the coordination of technical information services, particularly those provided by government departments and the principal research institutes for users within individual sectors of the economy. Research into information techniques and the training of information specialists would be among the tasks of this latter committee.

The recommendations of the OECD examiners for the organization of science in the government sector go most of the way with the NSC proposals¹⁰. The chief difference is that, unlike NSC, the examiners would not give full powers for resource allocation to the new board, although they do concede that the need for such powers might arise at a future date—presumably if their proposed mechanism is not fully successful. They are concerned that relationships be strengthened between government departments having a need for a scientific input to policy making, on the one hand, and the operational scientific institutes on the other. Second, they see the need to maximize the impact of scientific activities on the output of the Irish economy. Their proposals are designed to attain those aims in the context of Ireland's involvement in EEC.

The legislation needed to establish the new statutory board for science and technology is currently being studied, and action by government and parliament is expected before the end of the year. Hopefully, the full potential of Irish science will then be realized for the benefit of scientists and of society alike.

¹ *Endeavour*, 17, 3 (1958).

² MacCnámhain, S., *Eireannaigh san Eolalocht* (Oifig an tSoláthair, Baile Átha Cliath, 1966).

³ Meenan, J., and Webb, D. A., *A View of Ireland* (British Association for the Advancement of Science, London, 1957).

⁴ Murphy, D., *Ireland—Background Report on Science and Technology* (National Science Council, Dublin, 1972).

⁵ Murphy, D., and O'Brolcháin, D., *Research and Development in Ireland, 1969* (National Science Council, Dublin, 1971).

⁶ *Research and Development in Ireland, 1971* (National Science Council, Dublin, in preparation).

⁷ Lyons, T. F. R., and McCarthy, T., *Technology Ireland*, 4, No. 11, 14 (1973).

⁸ *Science and Irish Economic Development*, 1 (The Stationary Office, Dublin, 1966).

⁹ *Progress Report 1969–71* (The National Science Council, Dublin, 1972).

¹⁰ *Science Policy Formulation and Resource Allocation* (The National Science Council, Dublin, 1972).

MANPOWER

International Mobility Among Scientists

H. W. THOMPSON

St John's College, University of Oxford

Non-governmental bodies have an important part to play in bringing about increased scientific mobility. International cooperation can gain very much from goodwill among scientists.

THE intrinsically international character of science makes it logical that scientists from different countries should meet to share experiences, and compare methods in planning the further progress of science and technology. This is all the more important at the present time when science has a high responsibility to society, and when society must also act in a responsible way towards science.

Most international scientific cooperation is being directed to big projects, where the cost of equipment is high, and the duplication of facilities may be undesirable, and often impossible. Mobility among scientists—scientific interchange—is, however, perhaps the cheapest form of international cooperation, but it is also among the most effective. It is necessary because the scope and depth of scientific research today makes it impossible for most nations to provide all the facilities needed by their scientists. Of course, apart from any economic reasons, movement between countries has always been a recognized way of augmenting the training of research workers. The advantages do not rest solely with the individual, for on his return to his home country, his parent laboratory or institution gains from the broadening of his training and experience¹.

A few years ago, the Ministerial Conference of the Council of Europe adopted a resolution calling for more mobility in higher education and research in all fields². It is needed, of course, in the human and social sciences as well as in the natural sciences, but most of all at present in the natural sciences and technology where the speed of development is greatest. This is a modern manifestation of the movement of scholars and teachers which occurred many centuries ago.

Taking a broad view, international mobility of scientists occurs in a number of ways, which include: attendance at research conferences; through participation in the affairs of the international scientific unions or similar bodies; through work at international research institutes of one kind or another; and through visits by individual research workers to foreign universities or research laboratories for short or long periods. Each of these mechanisms has its specific value, but in my view the exchanges of working research scientists may be the most effective in the long term.

Conferences

International scientific conferences can be large, involving a thousand or more participants; or small, with only a hundred or fewer people taking part. During the past twenty-five years, the number of large conferences has increased rapidly with a corresponding increase in cost. Certainly these meetings

are often important and useful, but in my opinion their scientific value has become small, if judged against the cost.

By contrast, small specialized research conferences involving a hundred people or less, with a few selected main speakers who are expert in the field concerned, seem to me to have increasing scientific value; and especially if they take place in a relaxed atmosphere and when a previous decision not to publish the discussion stimulates free thinking and criticism. The Gordon Research Conferences of this type, started in the United States about twenty-five years ago, have proved outstandingly successful and have been followed in Europe during the past ten years by the EUCHEM conferences for chemistry, EUROMECH conferences in applied mechanics, and similar series in other fields, all organized voluntarily by international groups of working scientists themselves. There have been about fifty such small specialized EUCHEM conferences during the past eight years, covering a wide range of chemical topics, and held in different European countries. One is to take place in Spain this year. The intention and custom with such conferences is to operate at the minimum cost. Very often, they lead to continued contact and links between laboratories. The Council of Europe, and several private organizations, have given limited financial support to them, but they deserve to obtain greater and continuing help from public funds.

International Scientific Unions

During the past thirty years, many non-governmental international associations for different branches of science and technology have been established. They vary in purpose and effectiveness. Most of them are financed privately, but some receive help from governmental funds.

Perhaps the most significant is the International Council of Scientific Unions (ICSU) and its component unions, covering all the principal disciplines of natural science. Ninety-two countries now belong to the ICSU and its unions, being represented by their appropriate scientific body, usually the national academy, sometimes by a research council or other national organization.

It has been estimated that many (perhaps eight to ten) thousands of scientists from many countries are working voluntarily in commissions or groups of one sort or another for the ICSU and its unions. The unions themselves are concerned with work specific to their particular discipline. For example, IUPAC is concerned with international standards, nomenclature and terminology, agreement on analytical methods, criteria of purity of drugs and foodstuffs, and the compilation of reference data and chemical information. It has been advising the European Economic Communities for some years. It stimulates progress in chemistry by arranging symposia at intervals, and cooperates with other unions in a joint study of current problems in the teaching of science as a whole.

The ICSU itself conducts interdisciplinary studies on a world scale and it is also chief scientific adviser to UNESCO. In 1959, for example, it operated the global programme on the International Geophysical Year. During the past eight years,

the International Biological Programme has examined the biological basis of human welfare. It has studied the facts affecting organic productivity, the potential use of natural resources, and human adaptability in changing conditions. The results are still being evaluated. A natural consequence to this was SCOPE, a special committee set up to study problems of man in his environment, some time before this matter became a topic for governments, leading to the Stockholm Conference of 1972. SCOPE has considered all aspects of pollution, identified some important factors for study and control, and explored the scientific problems of an ecological community. It continues to advise the agencies established at Stockholm, and is linked also with the new UNESCO programme, Man and the Biosphere.

These are just a few examples of ICSU's work. Of course, in spite of its global character, the movement of scientists involved is not excessive, for most of the work is done at national centres and coordinated at periodic meetings, or by correspondence. Yet there is a considerable exchange of information and thought internationally, which creates a sense of contact.

It is doubtful whether the important role of ICSU and its unions, not only for science but also in creating valuable personal relationships, is always appreciated sufficiently by governments. The administrative structure is small in relation to the work done, and it is important that as costs inevitably rise, the modest financial support which such organizations need shall not be lacking. It is also desirable that more younger scientists should be brought into this work. This is primarily a problem of money, although the amount needed would be, comparatively, very small.

International Facilities

A third way in which mobility of scientists may be involved is provided by the international research laboratories or institutes, which are usually established and supported by inter-governmental funds. Lately, there seems to have been a wave of enthusiasm for them in some quarters, backed by well organized pressure groups. Certainly CERN, the nuclear physics centre at Geneva, is acknowledged everywhere as a great success, and has enabled workers from many countries to be trained and carry out work which they could not otherwise have done. Marine biological stations, such as that at Naples, are also valuable because biological specimens required for the work are available at the location. The Trieste Institute for Theoretical Physics has also been successful, especially in providing a centre to which scientists from developing countries could come for a period. The recently established Institute for Insect Physiology at Nairobi also appears to be doing well.

In my opinion, however, great caution is needed before large international laboratories are established. They are necessary when the cost of equipment is too high for any single nation, and costs must be shared; or when particular facilities make the choice of a particular location essential. They may also be justified if there is no alternative mechanism for the training of scientists in the existing national centres. Yet, apart from the high expenditure required, they involve some dangers, and even a possible disruption of existing successful national research centres. Sometimes, too, the large national financial contribution which is required may have a serious impact on the total science budget in the country concerned, and lead to an unbalanced scientific development.

Interchange of Scientists

I now turn to my last example of scientific mobility, although I think it is almost certainly the most important. It is the interchange of working scientists between centres in different countries, for shorter or longer periods. In my youth, after taking a first degree at Oxford, I went to Berlin to do research work, and took a doctorate there. The enormous change and

increased sophistication of modern research may now make movement at such an early stage of one's career much more difficult, and also less rewarding than it used to be. Exchanges at what may be called the postdoctoral level are more appropriate.

Exchanges can be either short term, say, up to two years, or longer term. Longer term mobility often involves a change of salaried employment in a place of higher education or research. In that case, a number of obstacles still remain, such as agreement about the equivalence of qualifications and eligibility for employment, the availability of work permits, the transferability of pension arrangements, sometimes in incompatibility of different national systems, the existence of restrictive national regulations, and difficulties of return later to the home country. Such difficulties need to be considered urgently by the international committees of university vice-chancellors and rectors, by national professional bodies, and by intergovernmental committees.

Short term exchanges are not subject to the same problems, and as I have said already, they are probably the cheapest among all major international scientific projects. Moreover, younger people can at once become involved in them. Visits abroad enable them to increase the rate of growth of knowledge, to enhance the quality and breadth of their training, to learn new techniques, improve their current awareness, and make contacts which strengthen the general scientific community. A leading French scientist remarked not long ago that the training of a research scientist is not complete unless he has spent a period, early in his career if possible, working abroad; and that he should later maintain contact with his professional colleagues in other countries. The fraction of the staff in universities and places of higher education and research who get this foreign experience is still not high enough.

Circumstances in Europe after 1945 were obviously not favourable for the movement of younger scientists. For this reason, there was a flight to North America, from which many did not return. Later, several agencies began to provide some support for exchanges, such as the national Research Councils in different countries, and intergovernmental bodies such as CERN, ESRO and more recently EMBO. Colleges and universities, however, even now have little money to promote such exchanges. Some private bodies, including the Humboldt Foundation and the Max Planck Society in Germany, provided travelling fellowships for scientists, although often only for foreigners to work in the country of the donor organization. Somewhat later, bodies such as the British Council and German Academic Exchange Service encouraged foreign exchanges at all levels, but the number of awards for research in the natural sciences and technology was insufficient.

A survey by the Royal Society of London in 1964-65 suggested that the total scientific exchanges in Europe was small, and not consistent with the resurgence of many excellent centres of research. After consultations with several of its sister academies and similar agencies in European countries, the Royal Society decided therefore to initiate a new scheme. This exchange programme started in January 1967, using private funds provided chiefly by the Ford and Wates Foundations. It provides for short study visits abroad, lasting a week to six months, and for fellowships lasting six months to two years. The response was so great that very soon the British government offered to make a more substantial grant to be used by the Royal Society, provided that a "balancing" mechanism could be established with the European partners. At the time, this "balancing" mechanism avoided difficulties of currency transfer, because the sending side paid the travel costs and the receiving side paid the subsistence, at agreed rates. This problem of currency transfer is less important now, but a partnership of this sort is still useful because the partners feel a joint responsibility and a continuing interest in the scheme.

The programme has grown rapidly, and today sixteen countries in western Europe are partners, namely: Austria,

Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and Britain. The adhering bodies are the academies in Austria, Finland, Ireland, Italy, Norway, Portugal, Sweden and Britain; in Spain the Consejo Superior de Investigaciones Científicas, in France the CNRS, in Germany the DFG, and corresponding organizations in the other countries.

This is a linked set of parallel bilateral arrangements in which each partner determines the scale of exchanges which it needs with the other partner, and can place emphasis on the particular fields of science that it prefers. Experienced scientists assess the applications, the sending side proposes and the receiving side is asked to approve, and the administration is minimal. There is little bureaucracy, quick decisions are made about applications for awards, and there is enough flexibility in the mechanism to ensure maximum success.

In six years, more than 1,500 awards have been made, covering all aspects of science and some aspects of technology. The number of awards has naturally been related roughly to the size of the country concerned. Not surprisingly, physics and chemistry are the most popular fields, but short visits for biological subjects seem to be very frequent. In 1972, the total sum spent was the equivalent of about £350,000. Last year, the British government decided to increase its grant to the Royal Society for this programme steadily during the next

few years, so that if other partners are able to make corresponding increases, the sum available in 1975-76 will exceed £600,000.

This programme is operated essentially for scientists themselves, and the partners meet only on one day each year to discuss progress and plan for the following year. It was initiated through private funds, and although now supported by governmental grants, is non-governmental in character. A recent study has shown that the programme now holds a leading place among all scientific exchange schemes in Europe³. Its growth during six years has been impressive, and lends support to the suggestion made in a recent report that such exchange schemes are probably best carried out by non-governmental organizations⁴. The British Council has recently obtained increased funds for use in Europe and may be able to expand its own exchanges of this kind.

¹ *Department of Education and Science Bulletin*, No. 2 (HMSO, April, 1969).

² Council of Europe, *CME*, 7 (71), 14 (1971).

³ Council for Scientific Policy, *Report of the Working Group on Scientific Interchange* Cmnd, 4843 (HMSO, 1972).

⁴ Council of Europe, *Obstacles to Scientific Mobility (Lesquillone Report)*, CCC/ESR (71) 11 (1971).

⁵ *Scientific Research in British Universities and Colleges*, 1, 2, 3 (HMSO, published annually).

FRANCE

Uncertainties in French Scientific Research

from *La Recherche*

With planning soon to start on the Seventh Plan, it is becoming clear that several of the policies enshrined in the Sixth Plan have been abandoned.

THE French elections of March 1973 have not had direct consequences for scientific research: Mr Jean Charbonnel remains at the head of the Ministère du Développement Industriel et Scientifique, which has in its charge the Commissariat à l'Energie Atomique (CEA), the Centre National d'Etudes Spatiales (CNES), and the Délégation Générale à la Recherche Scientifique et Technique (DGRST); and Mr Joseph Fontanet continues to head the Ministère de l'Éducation Nationale, to which pertains the Centre Nationale de la Recherche Scientifique (CNRS). Questions of scientific research were almost totally absent from the electoral debates, and there is nothing to indicate, at least for the moment, that research policy is among the pressing preoccupations of the new Messmer government. The uncertainties about the future of French scientific research which were so abundantly reflected in the research budget for 1973, a "zero increase" budget, remain.

At present it is discussions concerning the orientation of the CNRS and the regulations governing its research personnel which are on the agenda. The role of the CNRS in basic research has been growing in recent years. With more than 6,500 researchers and a total budget of the order of 1,500 million francs, the CNRS has in fact increasingly taken on the role of a pilot organization for basic research. This situation poses some problems, because the resources devoted to research in the universities by the Direction des Enseignements

Supérieurs de l'Éducation Nationale have been proportionally curtailed for several years, and thus the CNRS now controls most of the resources for basic research. The management of CNRS wants, on the other hand, to improve its relations with industry, which would permit it to provide outlets for some of its researchers while addressing itself to problems of industrial research. This is a rather uncertain scheme, because it runs against the traditionally sceptical attitude of industrial people to university research. The CNRS has nevertheless increased its efforts in this direction during the past year, in laboratories working on the "engineer-



Mr Joseph Fontanet



Mr Jean Charbonnel

ing sciences'', in order to develop certain lines of researches that have a close bearing on technological problems. This endeavour has been accompanied by the stated willingness of the directors of CNRS to redefine the regulations pertaining to its researchers. The principal objective sought in these reforms is to shorten the period of training for research (and therefore the time before submission of doctoral theses) and to make the end of this period into a turning point in the career of CNRS researchers, only the most capable being invited to pursue their careers in CNRS. Obviously, there is considerable opposition to such a reform, especially on the part of the researchers' unions, which see in these projects above all a means of institutionalizing penury. It is clear, however, that the debate about the education of researchers is quite fundamental, because the average age for completion of a thesis is now around thirty-one for researchers in the exact sciences. The future of basic research will depend to a great extent on the solutions which are found for these problems.

University research is also floundering in face of great organizational difficulties. The application of the 1968 law of Edgar Faure concerning the reorientation of the universities has in fact resulted, in those cases where both teaching and research is carried out, in a considerable excess of activity for teachers, and this seriously endangers the necessary equilibrium between teaching and research in a number of universities.

Atomic Energy

The other great problem of civilian research remains that of the broad scientific programmes in the realms of atomic energy, defence, and aerospace, which have long been considered as the chief motive powers of French science policy. The Sixth Plan has marked a very distinct evolutionary step in recommending a diminution of the share of these programmes in national defence research and development expenditure. The CEA has for its part started a move towards non-nuclear activities, with the setting up of an office for programmes of general interest and one for non-nuclear industrial cooperation. In 1972 the activities of these two offices represented 4% and 10% respectively of the civilian budget of CEA, and the directors intend to double the scale of such activities between now and 1980. It is clear that this attempt to realign part of the work of the CEA, which is pledged to put a ceiling on its budget (1,600 million francs in 1973 by comparison with 1,589 million francs in 1972), creates numerous problems, of which competition with other research organizations, public or private, is not the least.

Space Research

The situation at the CNES is in some ways similar to that of the CEA—especially as regards uncertainties about the future. French space policy, which had some successes during the 1960s, has not yet succeeded in finding a new orientation. In addition, French space policy is inevitably subject to the uncertainties of international space policy, because the international programmes of CNES account for about a third of its budget and thus exercise a serious constraint on its activities. It is well known that France has tried to persuade its European partners to construct jointly the rocket Europa III, but in the face of the reservations of its principal partners, Germany especially, France has prepared a modified project for the three-stage launcher L3S, which it may possibly carry out itself. (The cost of this launcher is estimated at 2,200 million francs against 3,100 million francs for Europa III.) No definite decision has been made about the L3S project (112 million francs have been designated in the 1973 budget for an eventual start), but it is clear that its financing cannot be borne solely by CNES. The departure from the Ministry of Defence of Mr Michel Debré, the most ardent advocate of the national launcher, raises serious questions about its future.

Meanwhile, CNES has to get by in 1973 with a total budget of 808 million francs, which is an increase of only 1% of that of 1972; this budget obviously does not permit it to engage in any new programmes.

Industrial Research

The Sixth Plan anticipated the according of a certain priority to industrial research, in particular to the procedures for stimulating such research by the state.

State support for industrial research, which represented 30% of the expenditure of industry on research and development in 1969, comes from several sources, in particular, the Ministère de la Défense Nationale, but it was specifically proposed to direct a greater proportion of state aid toward sectors such as mechanics, textiles, or chemical industry, which have up till now been neglected. The plan also recommended more prudence in the support to be given to the advanced technology sectors such as electronics. But in fact the recommendations of the plan have not been carried out by the government. Indeed, the money available for development aid has diminished by 50 million francs compared with 1972 and 85 million francs have been assigned to a "Plan électronique civil". This plan is designed to help a sector already "up", electronics, and is directed especially toward easing the difficulties of Thomson-CSF, contrary to the policy recommended by various experts. In continuing to devote an important part of its support for industrial research to the big companies the government is flying in the face of the policy of stimulating innovation in the small and medium-sized companies which was first recommended two years ago by the Ministère du Développement Industriel et Scientifique. In this area of science policy also, there is evidently a gap between certain proclaimed intentions and the policy actually followed. Even though one may be anxious for the future of industrial research in certain areas, notably in those affected by mergers, it seems that the financing of industrial research by industry itself has grown regularly for several years, for it has come to represent 36% of the national expenditures on research and development in 1972 by comparison with 32.5% in 1969. Thus French industry has, it would seem, respected the Sixth Plan.

The preparation of the Seventh Plan is to begin within a few months, even though many of the objectives of the Sixth Plan have already been abandoned. It is clear that over and above the problems of the financing of research it is the problem of the functioning of the institutions of science policy which is already on the agenda.

THE NETHERLANDS

Dutch Science and TNO

A. J. STAVERMAN

TNO, Juliana von Stolkerlaan 148, Postbus 297, The Hague 2076

One way in which international cooperation in research and development can be fostered is through organizations like TNO. This article discusses the work of that body in the context of Dutch science generally.

WHEN thinking about international cooperation between countries in Europe the first things to note are the marked differences in culture, mentality, history and attitudes between the countries concerned. These differences are surprising, for the peoples of Europe have been mixing through the centuries. Yet, in comparing countries like Italy and the Netherlands one immediately sees that they not only differ in population and area but in particular also in mentality and in the entire attitude towards life. Even neighbouring countries like Belgium and the Netherlands have a very different way of life and of dealing with public matters. So, if I start this article by giving some numbers to compare the Netherlands with other Western countries it is with the proviso that these numbers reflect the special features of the country only partly and perhaps indirectly.

Holland has a relatively small population (13 million) but a high population density (400 km⁻²). The level of science and technology may be described as high. This is not only the case in classic fields like civil engineering, especially building of bridges and waterworks, and agriculture, for the presence of Philips Industries means intense participation in modern fields of technology such as telecommunications, magnetic materials and computers. Given the small size of the country surprisingly many large industrial companies have their headquarters in Holland. As well as Philips there is also Shell, Unilever, AKZO, DSM and Hoogovens, to mention only a few.

The high level of technology is reflected in a large expenditure on research and development. As a proportion of GNP this was 1.9% in 1964, the same as France and surpassed by Britain (2.3%) and the United States (3.4%). If one considers only civil research and development, excluding military contributions, the Netherlands was nearly on a par with the United States (2.2%) in 1967 with 2.15% of the GNP and ahead of Britain (1.7%), France (1.6%), Germany (1.6%) and Japan (1.4%). Also as regards the total manpower in research and development as a proportion of the civilian labour force, the Netherlands (1.14%) was in 1967 second behind the United States (1.85%) and far ahead of France (0.99%) and Britain (0.91%) whereas technologically well developed countries like Sweden (0.67%) and Switzerland (0.78%) are even further behind. Of course, the small distances in the country are very favourable to the research and development climate which depends on intense communications between specialists of all kinds and ranks.

From its geographical situation and from its size the Netherlands has grown accustomed to think and act internationally in many ways. No industry can exist in Holland without a

foreign market which is often many times larger than the domestic market.

Research Institutions

In a thorough report on the situation of research and development in the Netherlands¹ the OECD examiners expressed their surprise about the presence in the country of a number of large laboratories such as the Hydraulics Laboratory at Delft, the Laboratory for Shipbuilding in Wageningen, the Aerospace Laboratory at Amsterdam and the Reactor Centrum Nederland (RCN) in Petten, some of which have a good international reputation and attract many contracts from foreign countries. The examiners concluded that "it seems that these examples of national facilities reveal a difficult problem. How can a small industrialized country develop modern tools in research and development for sectors in which the critical mass exceeds the needs of the nation? The financial load may become prohibitive and, in addition, an unhealthy working climate may develop if no use is made of these facilities. International collaboration seems inevitable but with a plan for specialization that assures that each country is not developing the same tools. How can a public financial effort, conceived for a national purpose, be justified within such an international setting?"

Obvious as this statement may sound, something must be fundamentally wrong with it. Indeed the first three of the four laboratories mentioned above have developed their international reputation from selling their services throughout the world on the basis of bilateral contracts, whereas the RCN has from the beginning relied heavily on the formal international collaboration in the Euratom organization. The difficulties suggested by the OECD examiners have always been and still are much more evident in the case of RCN than of the other laboratories. This is, of course, a consequence partly of the unfortunate political troubles which gradually destroyed Euratom and partly of the particular course that the development of civil atomic energy has taken throughout the world. But in any case one should consider with caution and suspicion any all-too-easy conclusions from the OECD report such as "Before starting a high level research laboratory in any field, small nations should make sure this laboratory fits within a framework of formal international collaboration".

Generally, small nations are handicapped by their size in many ways, not only in research and development but also in industrial production, trade, services and even in environment control, because very often their home market is too small to support a full size enterprise and every foreign market can be closed or manipulated by government actions outside the control of the nation in question. The answer for the small nation is, however, not to wait until formal international collaboration has been established but to look for openings in the international markets and fill those vacancies with products of the highest attainable quality. This is, at least, the situation in the West today and very probably for the next few decades as well.

Like any handicap this one is also compensated by several factors. Once the necessity of international contacts has

become apparent the whole world is open to the small nation as a potential market. With regard to research and development contracts in a small nation an institute is probably less hindered than it would be in a large country by objections from national industry to accepting contracts from foreign industry. The Dutch government-supported research organization TNO, which will be discussed more fully later in this article, accepts exclusive contracts from foreign industries and governments, after giving a right of first refusal to the national industry if there is an appropriate one.

Of course, the fact that in practice bilateral, contract-based international cooperation has so far been more efficient than formal international collaboration does not imply that this will not change in the future. Generally the Netherlands has played and will continue to play an active part in projects of international collaboration in research and development such as the ultracentrifuge project, the fast reactor project and others.

Once formal international collaboration has been started in a new field this may strongly affect the programme of national research institutions. It is therefore important that such institutions have sufficient flexibility to adapt themselves to changing circumstances, whether in the way of international collaboration or of a change of the market.

TNO Organization

The flexibility of a laboratory can be severely restricted by the "mission" it acquired at its foundation. If the market changes the original mission may become obsolete or less important whereas attempts to enter new fields may meet resistance from institutions with other missions. It must therefore be considered as a very fortunate decision of the Dutch government in 1932 not to found a research organization with a definite field of research but to found the Organization for Applied Scientific Research TNO (Toegepast Natuurwetenschappelijk Onderzoek) with the purpose "to foster the efficiency of applied scientific research", as it was stated in the TNO law of 1932.

At that time the importance of scientific research for the community at large was much less clear and accepted than today. Therefore the decision in 1932 must be considered as very far sighted. By the creation of TNO a meeting place was provided where scientists could look for information on the needs of the society and the community could look for advice from science. It is important that although the budget of TNO is guaranteed by the government the organization itself is independent, not forming a part of the government, and with employees of its own who are not government officials. In this way sufficient separation from political pressures and from involvement with government policy is maintained. Of course, government officials are members of the central board and most of the divisional boards of the organization, but they are always a minority among the representatives of industry, science and public institutions. So in the research and development policy of the government does not have very much effect on TNO although the ultimate financial control rests with the Ministry of Finance.

As stated earlier, one of the very strong points of TNO has always been that it is not mission oriented; any branch of science considered of sufficient importance in the context of application in any branch or activity of the community can be incorporated in the TNO organization without the necessity

of founding new institutes, buildings and pension schemes. Although this situation has not remained completely unchallenged the existence of TNO it is still a strong point today in a world that is much more conscious of the importance of science for the community and changing much more rapidly than 40 years ago.

Part of the challenge to the freedom of TNO came from the necessity to organize research in units with a coherent purpose. This led first to the foundation of suborganizations of TNO (the NO for industry, trade and traffic, the GO for health, the VO for food, the RVO for defence and the LO, which later separated from the TNO organization, for agriculture. Under the auspices of each of these suborganizations there are several institutions, laboratories and working groups, each with a more or less specified mission. Yet the freedom of the organization as a whole to initiate or stop research in specified fields is much greater than would have been the case without the TNO framework.

Another challenge to the TNO philosophy has been the foundation of new mission oriented research institutions without taking advantage of the existence of TNO. Examples are the large National Organization for Agricultural Research which split off from TNO but still cooperates closely, and the Reactor Centrum Nederland, working in the field of nuclear energy, which also cooperates with TNO. The existence of institutions for applied research not belonging to TNO does not, however, strongly affect the freedom of TNO to choose its research projects. Of course, it means that the budget of TNO is only a part, and rather a small part, of the total effort in applied research of the country.

Table 1 Size of TNO

	CO (central)	NO (in- dustry)	GO (health)	VO (food)	RVO (defence)	Total
No. of employees	711	1,853	749	430	654	4,397
No. of graduates	135	269	153	80	132	769

I shall now quote some figures. Table 1 shows the number of employees and of graduates in the organization. Table 2 gives the budget of the organization as a whole and of the suborganizations appropriately divided. Table 3 shows the expenditure on research and development in the Netherlands in 1971 divided according to source and destination. These figures are given in Dutch guilders, Hfl. 1 being about \$0.34 (about £0.14). Table 3 demonstrates that the budget of TNO constitutes only a small fraction, in fact less than 1%, of the national expenditure on research and development and less than 35% of government expenditure on research outside the universities. Yet Hfl. 200 million is not a negligible sum and 4,400 employees including 769 graduates are not negligible either as a research team that can be directed quickly towards the solution of new problems turning up in the community.

To give an example, many TNO institutes from various suborganizations work on problems related to control of environment, while the central TNO organization has created a Commission for Environmental Research and a Study Centre for Environmental Research. These institutions are very useful in regulating the flow of information on environ-

Table 2 Budget of TNO, 1969 (Hfl. million)

	CO (central)	NO (industry)	GO (health)	VO (food)	RVO (defence)	Total
Direct government subsidies	11.7	40.7	17.5	8.0	25.9	103.8
Outside orders	7.9	19.9	4.5	4.2	1.9	38.4
Outside contributions	0.5	5.0	2.5	1.7	1.1	10.8
Total	20.1	65.6	24.5	13.9	28.9	153.0

Table 3 Expenditure on Research and Development in the Netherlands in 1971 (Hfl. millions)(from ref. 1)

I Government expenditure	
Education and science	629
Research and development missions, including TNO	488
International contributions	53
Industrial projects	70
Total government	1,240
II Industrial expenditure including government support of industry	
The "big five"	1,020
Others	700
Total industry	1,720
Total industrial expenditure excluding government support	1,650
Total expenditure on research and development	Hfl. 2.89×10^9
Total TNO budget	Hfl. 0.2×10^9

mental problems on the one hand, and on the results and prospects of research for the entire country on the other. Also in many cases where technical aid is requested by a developing country TNO can assist in finding or providing the technical specialists for the job. And in many international projects in which the Netherlands participates, TNO provides one or more national representatives.

I would by no means suggest that the TNO model for organizing research is advisable or the best for some or most other nations. But one can say that, in spite of much criticism which has been launched over the years, the Dutch are happy with the TNO organization as an efficient and flexible tool in adapting the research potential to the needs of the nation and are grateful to the remarkable foresight of those who founded it 40 years ago.

¹ *Reviews of National Science Policies, Netherlands* (OECD, Paris, 1972).

GERMANY

Research in the Federal Republic of Germany

JULIUS SPEER

Deutsche Forschungsgemeinschaft, Kennedyallee 40, 5300 Bonn-Bad Godesberg 1

The president of the German Research Society describes how scientific research is carried out and financed in the Federal Republic of Germany.

SCIENTIFIC research in the Federal Republic of Germany is carried out at government, semi-public and private research institutions. In addition, research is done to a limited extent by individuals, for example, for the annual "Research by Youth" competitions or in connexion with other projects encouraged by awards and prizes.

Government and Government-supported Establishments

In accordance with the Basic Law applying in the Federal Republic, national competences in the sector of science policy are divided between the Federal Government and the Länder. In accordance with Articles 30, 70 and 83 of the Basic Law, competence with regard to legislation and administration is in the first instance incumbent on the Länder. In accordance with Article 74, point 13, however, the Federal Government was, from the outset, equipped with extensive powers with regard to concurrent legislation, which were later, for example, extended to cover the field of the production and utilization of nuclear energy (Article 74, point 11a of the Basic Law). Parliamentary committees for dealing with science matters exist at parliamentary level both within the German Bundestag and also within the Länder parliaments.

At the Federal level there is a Cabinet Committee for Scientific Research, Education and Promotion of Training (Committee of Ministers), and at the level of government experts an interdepartmental Committee for Science and Research. Both committees deal with fundamental questions of science and research policy, and coordinate the Federal Government's promotion measures. The Länder governments

have their Permanent Conference of Ministers of Education.

Administrative agreements have been concluded between the Federal Government and the Länder with a view to establishing a joint research policy. As a result of these agreements, joint bodies are appointed and financial matters are dealt with. By the Administrative Agreement of June 4 1964 (extended on February 8, 1968), a permanent commission was established by the Federal Government and the Länder for reciprocal information and the coordination of the financial promotion of science and research. An administrative committee was also created for the scrutiny and fixing of the grants to be provided annually by both the Federal Government and the Länder for the German Research Society and the Max Planck Society. The Science Council was also created as a result of an administrative agreement in 1957, as a joint advisory body of both the Federal and Länder governments, for dealing with scientific and research matters.

According to this administrative agreement, the Science Council has the task of drawing up an overall plan for the promotion of science. In so doing, it must also coordinate the plans submitted by the Federal and Länder governments with one another, and also establish priorities and degrees of urgency. Furthermore, the Science Council must present a programme of urgent tasks each year, and make recommendations as to how the promotion funds provided by both the Federal and Länder governments should be used. The Science Council is composed of members of the scientific and administrative commissions.

Since this year, responsibility at government level for science and research policy has rested with the Federal Minister for Education and Science, and also with the Federal Minister for Research and Technology, together with the relevant government departments. At Länder level, the ministers of education are responsible, in some cases the ministers for research, and the relevant Länder government departments.

All government competences from the pre-primary school to university, including vocational training, are in the hands of the Federal Ministry for Education and Science. This also includes the promotion of science at universities in close

collaboration with the Federal Ministry for Research and Technology.

The competence of the Federal Ministry for Research and Technology embraces general research promotion measures—excluding the German Research Society and the centres of excellence which, on account of their link with universities, have been assigned to the Federal Ministry for Education and Science—research planning and coordination, technological research, development and innovation, nuclear research and technology, and competence for establishing principles and coordination for both civil and military aerospace research and development. In addition, the Ministry for Research and Technology has been given competence by the Federal Ministry of the Interior for the “data bank system” working group and also for the coordination of Federal Government information systems. The Federal Minister of Economics and Finance has transferred his competence for the promotion of electronic data processing to the Federal Ministry for Research and Technology, and finally the latter has received competence from the Federal Ministry for Youth, Family Affairs and Health for the “German Cancer Research Centre” foundation at Heidelberg.

In addition to both ministries dealing directly with education and research, promotion of research is dealt with in particular by the Ministry of Defence, the Ministry of Economics, the Ministry of the Interior and the Ministry of Food, Agriculture and Forestry. Environmental matters are, for example, concentrated at the Ministry of the Interior.

Federal Institutes

The Federal Government maintains—as do to a lesser extent the Länder—a number of its own research establishments. The organization of these establishments is a task for public administration, and each institute answers to the respective minister for the purposes of departmental research. Among these establishments are the Federal Health Office in Berlin, the Physico-technical Federal Institute at Brunswick, the Federal Institute for Materials Research in Berlin, the German Hydrographical Institute at Hamburg, the Agricultural Institute in Brunswick-Völkenrode, the Federal Institute for Regional Geography and Physical Planning in Bad Godesberg, the Federal Institutes for Hydraulics and Hydrography at Coblenz, and the Federal Institute for Telecommunications Engineering at the Central Office of the Federal Postal Services at Darmstadt. These institutes do not restrict themselves solely to providing scientific aid for administrative activities and the tasks of the authorities, but to some extent also carry out fundamental research work. The work of several institutes has a direct bearing on industrial and technical development, as, for example, the Central Office for Telecommunications, or the Federal Institute for Soil Research, which devotes its activities to discovering and opening up deposits of raw materials in close cooperation with industry.

Autonomous Organizations Promoted by the State

Ten big science institutes have been created as autonomous organizations by the Federal Government and, in part, by the Länder. These institutes carry on scientific and technological research and development, to the extent that the execution of such work poses unusually great requirements as regards staff, funds and equipment exceeding certain limits. Among them are the Hahn Meitner Institute for Nuclear Research Ltd at Berlin (HMI), the German Electron Synchrotron at Hamburg (DESY), the Association for Heavy Ions Research Ltd at Darmstadt (GSI), the Nuclear Research Centre Ltd at Karlsruhe (GFK), the Jülich Nuclear Research Establishment (Ltd) (KFA), the Association for the Utilization of Nuclear Energy in Shipbuilding and Shipping at Hamburg (GKSS), the Max Planck Institute for Plasma Physics at Garching (IPP), the

Association for Radiation and Environmental Research Ltd at Neuherberg (GSF), the German Aerospace Research and Testing Institute at Porz-Wahn (DFVLR), and the Association for Mathematics and Data Processing Ltd at Birlinghoven (GMD). The individual big science establishments deal with varying tasks. They are partly centres for basic research, partly research and development centres engaged on a large number of different projects, programmes and specialized areas.

In order to facilitate the desired possibilities of organization, the legal forms of the said government research establishments are, in addition to public institutes, non-independent institutes under public law, legal organizations under civil law, registered associations, companies with limited liability, or foundations having legal status. Where big science establishments are concerned, the form of limited liability company is chiefly chosen.

Academic Research

Academic research is carried out in a wide range of fields at universities by persons who work full-time or part-time there and make use of the equipment, means and services available. The universities are a matter for the individual Länder, and are either autonomous establishments of higher education, or in varying degrees of transition towards becoming part of larger organizations as comprehensive universities. Academic research serves to provide a scientific foundation for the selection of study subjects, the scientific further development of such subjects, the scientific dissemination of knowledge and as an introduction to research work (research-oriented learning). Non-application-oriented research (basic research), which can also be carried out cooperatively as project-oriented research or interdisciplinary research, is most suited to university purposes.

As a rule, academic research is carried out by research workers who receive emoluments from the government as civil servants or by government employees at government research establishments. Research at universities is distinguished from publicly supported extra-mural research in that legislation accords the universities extensive powers of self government. This is intended to guarantee considerable freedom of choice of subject and a diversity of orientations and methods for groups and individuals.

On the other hand, researchers at universities are usually engaged as teaching staff, meaning that they can only devote their energies to research in a limited degree. The compulsion to present methods and results provides both an excellent impulse for further development and ensures that scientific findings are made widely known. To the extent that university training has to be scientific, the institutional link with research is indispensable. In order to carry out research at universities, the following requirements must be met: the right to practise research as an integral part of the scientist's official duty to engage in scientific work; allowing the individual time in which to do research work; provision of the institutions with basic aids for research; and the right of the researchers to procure additional funds for research purposes.

Academic research varies. As a rule, however, it is organized as follows: a central level, with a Research Commission which is competent for distributing central research funds, and, in addition, is particularly responsible for the interdisciplinary orientation of the research institutes. Then there is the level of specialized branches of study, where the staff are primarily responsible for organizing the training offered. Within the disciplines, or parallel to them, are departments, institutes, working groups, project groups and similar bodies. The latter have their own budget and their internal self-administrative system, and, as well as carrying out training programmes, they are responsible for research.

In 1968, at the recommendation of the Science Council, a start was made on the establishment of centres of excellence at the universities in compliance with the respective applications

from such universities. These centres of excellence are to provide more efficient research units at universities, facilitate intensified financial promotion and an efficiency survey, encourage cooperation between research workers and the various research institutions, and establish well planned priorities.

Max Planck Society

The Max Planck Society for the Advancement of the Sciences, which is financed chiefly by the Federal and Länder governments, carries out selective research in fields which are of particular scientific importance or "future oriented". The activities are pursued in the society's own special institutes, some of which are extremely large, and particularly high qualitative demands are made of the scientists working there. The natural science sector is given priority, and the bulk of the work done is devoted to basic research.

German Research Society

The German Research Society uses the funds made available to it by the Federal and Länder governments and the Donors' Association for German Science chiefly for the promotion of research projects drawn up by German scientists, and for the promotion of young scientists. In addition, the society supports cooperation among researchers and research planning in the Federal Republic. It counsels parliaments and governments on scientific questions, and in particular fosters the contacts between German research work and scientific activities in other countries too. Decisions are taken on a democratic basis by the experts elected by scientists and the representatives from the Federal and Länder governments. As a matter of principle, promotion is given to all sectors of science, and is directed first and foremost to research carried out at universities.

Fraunhofer Society for the Promotion of Applied Research

The Fraunhofer Society for the Promotion of Applied Research is a sponsoring organization in the sector of applied research. It has the task of facilitating the handling of scientific and technical problems of applied research, and, at the same time, of providing adequate scope for the initiative of individual scientists in this field (application-oriented basic research and contract research).

Academies

The five science academies in the Federal Republic (Düsseldorf, Göttingen, Heidelberg, Mainz and Munich) execute projects covering longer periods of time, exceeding the lifetime of a researcher. In addition, they constitute a forum for colloquia or symposia on topical scientific themes in which a small group of scientists participates.

International Participation

The Federal Government participates in a number of international organizations in the sector of research and development. A distinction must be made between organizations possessing their own research capacity (Euratom, CERN, ESRO, ELDO and so on), organizations with tasks in the field of promotion and coordination (for example, the OECD), individual international projects (for example, the Fast Breeder project and the Symphonie telecommunications satellite). International cooperation is in the throes of growth. Particular importance is attached to the fairest possible distribution of both benefits and burdens.

Non-governmental Research

This is industrial research, which must be defined as research aimed at creating new products. As a rule it is oriented to

the goals of the individual enterprises, in order to guarantee their competitiveness and place in the market. It is devoted to research and development and aims at producing an economic profit. A distinction is made between the following. (1) Individual research carried out by enterprises themselves. This is the usual form of research pursued, and has been developed mostly by the steel, mechanical engineering and automobile industries, electrical engineering and the chemical industry. (2) The issuing of licences and specialization agreements, facilitating a kind of division of labour for the participating firms. (3) Industrial cooperative research carried out by research associations of branches of industry in jointly sponsored research centres, or as jointly financed contract research. Advisory committees composed of representatives of the member firms and of scientists discuss the research programmes which, in the opinion of both scientists and those engaged in industry, have priority for the respective branch of industry in each case. Development up to the production maturity stage is carried out by the enterprises themselves. Seventy such associations are grouped together in the Confederation of Industrial Research Associations (AIF) at Cologne. The industrial groups less oriented towards research (for example, mining, foodstuffs and semi-luxuries, leather goods, textiles, timber, paper and printing, quarrying, earths, glass) play the principal part in this. (4) Contract research is research which is carried out on the basis of an agreement concluded between the contract-awarding party and an individual scientist, research institute or another enterprise as the contractor. A special form is the procurement of expert opinions. Contract research can solve problems caused by bottlenecks in staff, funds or equipment. Contract research resulted in the establishment of the Battelle Institute and in the development of the Faunhofer Society as a sponsoring company. Cooperation between industrial research and government-supported research institutes can also be effected by way of consultancy contracts.

Funding of Research

In 1971, public expenditure on science amounted to DM 13,500 million. Of this sum, it is estimated that DM 8,000 million—1% of the gross national product—was spent on pure research projects. Research expenditure on the part of industry amounted to approximately DM 7,700 million, and was, therefore, almost as much as that spent by the government. Altogether, then, about 2% of the gross national product was spent on research and development.

Public funds, excluding private grants, contract fees and proceeds from capital, are distributed to a varying degree between the Federal and Länder governments. A rough estimate is shown in Table 1.

Table 1 Distribution of Funds for Research and Development

	Federal Government %	Länder or host land %
Federal research institutions	100	—
Länder research institutions	—	100
Big science establishments	90	10
Basic equipment for university research	10	90
Max Planck Society	50	50
German Research Society	50	50
Academies	—	100
International research institutions	100	—

Private expenditure on science stems chiefly from the industrial firms interested in such projects. In addition, donations and contributions in kind are given by both private individuals and private organizations and foundations for research purposes, for example, by the Donors' Association for German Science, by the Volkswagen, Fritz Thyssen, Bosch and Krupp Foundations, and organizations of a similar nature.

SPAIN

Spanish Science in a Dilemma

by our Special Correspondent

A meeting held in Madrid last month highlighted one of the chief problems with Spanish science—whether to concentrate limited resources on buying in technical knowledge or to establish a really viable Spanish research capability.

THERE is little doubt that Spain is making great efforts to improve its scientific image. Not the least of that country's attempts to improve the quality and organization of science was the recent meeting held in Madrid under the auspices of the association of scientists who work for the Consejo Superior de Investigaciones Científicas (CSIC), the Higher Council for Scientific Research. This meeting, which even a decade ago could not have been envisaged, focused attention on the problems of Spanish science by comparison with the way in which developed and other developing countries organize their science.

But what are the chief problems with the organization of science in Spain? Clearly one of these is the shortage of money. Spain, in 1972, spent 0.4% of its gross national product on research and development, a figure similar to that spent by Iceland but which compares unfavourably with the 1.4% spent by Japan, 2.4% by Britain and a mammoth 3.0% by the United States, these latter figures being for 1970. In terms of hard cash Spanish industry in 1972 spent 5,000 million pesetas (£35.7 million) on research and development, 2,000 million pesetas more than it did in the previous year, which itself was double that spent in 1967. But all the same, Spain spent 13,000 million pesetas in 1972 in payments for foreign technology. Although this staggering deficit of 8,000 million pesetas did not increase between 1971 and 1972 it has gone up from a more modest value of about 6,000 million pesetas since 1967–68.

Where Research is Done

Traditionally, research in Spain has been carried out in research centres and not in universities, although the situation has changed to a certain extent in the past ten years. In 1967, according to the OECD¹, 52% of the total expenditure on research and development in the country was spent in government research centres, with the bulk of the remainder, 43.4%, being spent in industry. Only 3.2%—106 million pesetas in 1967—was spent in higher educational establishments, with 0.9% accounted for by research associations.

The shortage of money for research boils down to the basic fact that Spain spends as much a year on research within the country as it does in buying patents, licences and "know-how" from abroad. In this respect Spain compares most unfavourably with other countries. Figures for 1967 show that for each peseta spent on research and development in Spanish industry four pesetas were spent on licence payments. Italy, on the other hand, spent 30% more on internal research in industry in 1965 than it spent on external licences, while in 1967 Japan

spent four times as much on industrial research as on licence payments. France, Germany, Belgium and Sweden all had a much healthier ratio of money spent on internal research to money spent on external licence payments.

The soul searching that is now going on within Spain is about whether or not Spain should continue to increase the sums it spends on external licences to improve rapidly the efficiency of its industry, basically following the plan which has made Japanese industry such a force to contend with in the past decade. It is accepted within the country that such a method of approach will be good in the short term, but what will be the long term effects? Japan, in fact, spent much more on external licences in 1967 than any other country (\$251.5 million, twice what it spent in 1965) but in both 1965 and 1967 it spent four times as much on industrial research at home.

On the other hand, it is recognized that provision of a substitute for knowledge imported from abroad would necessitate the spending of much more money on research. The equation is not, however, balanced by these factors for there is no doubt that an increase in home research will lead to better trained scientists and technologists and a better standard of research in the long term.

Which Way?

But time is fast running out and some decision must be made soon within Spain about which way the country must turn and how it should concentrate its efforts in the coming years. Last year a detailed plan for the reform of the administrative structure of research was called for, which is symptomatic of the realization within Spain that science and technology must play a large part in the future development of the country.

It is clear that Spain cannot afford to drop completely its dependence on foreign technology and there is therefore an evident need to establish priorities in some research fields. A balance must be established between creating technology within the country and importing knowledge from abroad, with the aim of eventually halting the increase in the sums of money spent on foreign technology. The question which must be answered is what fraction of Spain's limited resources should be spent on developing long term applied research at home and how much can sensibly be spent in buying technology to make Spanish industry immediately viable?

Spain must also decide in the near future whether it is a good thing that most of the universities are divorced from meaningful research. Since the CSIC was set up in the late 1930s most of the pure research within the country has been carried out at research institutes attached to the Higher Council for Scientific Research. It is only in isolated instances that research groups have been set up in the universities, and this has happened only comparatively recently. But can a university fulfil its purpose without the involvement of the academic staff in research? At the meeting in Madrid last month this question was aired several times. The purpose of the universities is to teach, said some participants who were employed at CSIC research institutes, and the research should be left to CSIC establishments. But, countered others, a university is a place for furthering knowledge and this cannot be done effectively without the active participation of the teachers in research. That the

officials of the CSIC are aware of the problem became clear in Madrid when Dr Federico Mayor, the acting president of the CSIC, said that it was essential that the universities and the research council centres should be brought closer together.

University Outlook

There are at present twenty-seven universities in Spain, of which three are private establishments with the remainder being supported by the state. Three of these state universities, those at Santander, Cordoba and Extremadura were first funded in 1972 and 1973. In all about 250,000 students attend Spanish universities.

The teaching staff at the universities are, broadly speaking, divided into Catedráticos, Agregados and Adjuntos, which are the equivalent of professors, readers and lecturers respectively in British universities. There are about 1,500 Catedráticos and Agregados in the universities and more than 3,000 Adjuntos with something of the order of 2,500 to 5,000 staff lower on the scale.

Although most of the pure research in Spain is carried out at research institutes it is estimated that some 30 to 50% of the staff at the universities carry out research. But a great deal of this cannot be considered front line research. The funding of research within the universities comes from two sources. The universities themselves contribute about 500 to 1,000 million pesetas a year, while the Ministerio de Educación y Ciencia supports about 500 staff to the tune of about 250,000 pesetas each. Thus the university supports its own research to a much greater extent than the government does. The fellowship programme of the Ministry of Education and Science has been one of the successes of recent years in Spain. Each graduate student is now awarded 120,000 pesetas a year while the department in which he is studying is also awarded a similar amount by the government. In all about 900 million pesetas are spent supporting graduate students in this way.

But why has research in the universities been slow to build up in spite of encouragements offered to the staff in recent years? Perhaps the chief reason has been the relatively low salaries paid to university staff until comparatively recently. This forced a substantial proportion of the staff to spend only part of their time at the university. Another contributory reason was that the equipment available at the universities to carry out research was of a low quality and this did not offer any inducement to the staff to start research projects. But the position is now changing. The staff are better paid and money for research is more easily come by. Thus the university staff can be expected, as time progresses, to spend more and more time at the university. In particular the hope is that the staff in the medical faculties will spend more time at the university carrying out research—it is the members of these faculties which are mostly under attack for spending little time on the university campus.

Questions of Staffing

The traditional method of choosing staff for universities in Spain is by examination, but in the late 1960s an innovation was introduced that allowed universities to appoint some members of staff on a contract basis for periods of up to five years. In 1968 a new university, the Universidad Autónoma de Madrid, was set up and one of its features is that 90% of the staff are on contract; only 10% were appointed by the traditional method and thus have tenure. Other universities in the country also have staff on contract but they have many fewer such members than the Autonomous University.

But this innovation which was at first greeted with great enthusiasm in Spain and by Spanish scientists working abroad, is in danger of turning sour. For one thing the people on contract were first of all put on the same salary scale as tenured professors, readers and lecturers (Catedráticos, Agregados and Adjuntos), but since July 1972 the salaries of the traditionally appointed professors have been 30% higher than the salaries of

those on contract. There is also concern, now that the initial five year period of the plan is coming to an end, that the contracts of some members of staff will not be renewed, or that they will be offered inferior terms.

There have already been difficulties at the Autonomous University in Madrid over the contracts of some junior people when they came up for renewal in October 1972. The new contracts presented were, according to the faculty members, unsatisfactory, but following discussions with the rector the contracts were changed. In March 1973, however, the staff members had still not received their completed contracts from the university authorities and they therefore took strike action last month. The strike was short lived but staff members who took part have been penalized by loss of salary in some instances and by suspension in others.

Needless to say, the effect on the morale of the staff on contract has been bad and it is sad to think that a successful experiment is in danger of failing because of administrative difficulties. There is little doubt that having staff on contract has enabled the Autonomous University to build up quickly viable research groups that are competitive with any in Spain—or any other country for that matter. It would be a tragedy for Spanish science if the research groups staffed by faculty members on contract at Spanish universities were made less effective because of the difficulties and problems of the past eight months.

The fear is that the scheme to appoint faculty members on contract will be abandoned and that Spanish universities will revert to choosing their faculties by the traditional methods. This would in all probability mean the splitting up of the larger departments built up under the new system into smaller and less effective units; one consequence would be that the import of new blood would be made more difficult. Ultimately those Spanish born scientists who have been seduced back to Spain by the advantages of the contract method of appointing university staff may once more leave their native land to practise their professions abroad.

Differentials

The administrative difficulties with Spanish science are, however, not all restricted to the universities, and a justifiable complaint of the scientists who work for the CSIC is that their salaries also are less than the salaries of the tenured staff at the universities. Another complaint, which emerged at the recent meeting at Madrid, is that some research institutes of the CSIC receive preferential treatment, and that while some institutes are struggling to carry out research on limited budgets others experience no such difficulties. But the reasonable answer to this, given by Dr D. Jose Llado, the deputy chairman of the CSIC, is that resources must be concentrated in areas where they will reap the greatest return—because of an overall shortage of funds—and this means that some institutes will be better off than others.

But the Spanish scientists must have a method of assessing whether or not the decisions taken to support one research institute to a greater extent than another are justified. More openness in decision making will be very much appreciated and the signs are that with the appointment of Dr Federico Mayor as acting president of the CSIC confidence will be built up in the administrators of science.

There is, however, little doubt that Spanish science could soon be a force to be reckoned with if the present trends are allowed to develop. The success of last month's meeting in Madrid is an encouraging sign. The discussion of science and science policy within the country that took place at the meeting shows that there are enough people prepared to debate the merits and disadvantages of various courses of action. This will ensure that the issues will at least have an airing before far reaching decisions are taken about the future of research and development within Spain.

¹ *Reviews of National Science Policy, Spain* (OECD, Paris, 1971).

Oxidation of Acrylic Fibres for Carbon Fibre Formation

A. J. CLARKE & J. E. BAILEY

Department of Metallurgy and Materials Technology, University of Surrey, Guildford, Surrey

The oxidation stage in the production of carbon fibres from acrylics is time-consuming. Here we describe why oxidation is necessary.

THE production of high strength and high modulus carbon fibres from any precursor requires the formation and retention of molecular orientation. Highly oriented acrylic fibres are very suitable starting materials because if certain precautions are taken during carbonization, chain scission and loss of molecular alignment occur to only a minor extent so that acceptable high strength and high modulus carbon fibres may be produced directly.

What are the precautions taken during the carbonization of acrylic fibres in order to prevent chain scission and loss of molecular alignment? The fibres are heated in an oxidizing atmosphere, while under mechanical restraint. It was the latter condition that enabled Watt, Phillips and Johnson to take out the patents for the production of high strength and high modulus fibres¹ after Shindo had previously produced carbon fibres from basically the same polymer system², without ensuring that molecular orientation was retained. But the question remained—why is oxidation so necessary?

Typical conditions for the preparation of high strength carbon fibres from 'Courtele' acrylic fibres are: oxidation under mechanical restraint in air at 200° to 225° C for 2 to 10 h, followed by carbonization in vacuum or inert atmosphere, not under restraint, at a heating rate of 1° to 2° C min⁻¹ to 1,500° C. These fibres may then be graphitized by heating at 1,800° to 2,500° C for 1 to 2 h under vacuum, which produces the high modulus fibre.

Here we describe an extension of previous work³, an attempt to analyse by infrared spectroscopy and elemental analysis, the reactions occurring during oxidation.

Before the advent of high performance carbon fibres, acrylic polymers aroused considerable interest in the textile industry because of their thermal colouration reactions. Houtz, using the concept of ladder polymer structure, was the first to attempt an explanation of these reactions⁴ (I) in which atactic polyacrylonitrile (Ia) cyclized to give "ladder" structure (Ib). After Houtz, most papers have referred to the formation of ladder polymer when acrylic polymers were "degraded" in inert, oxidizing or alkaline conditions⁵⁻¹⁸. There are, however, considerable differences in the proposed chemical structure of the ladder polymer, particularly after oxidation. Three principal structures for the oxidized polymer have been proposed.

Structure II was suggested after infrared and elemental analysis of the oxidation, and shows oxygen present in the form of bridging ether type groups¹⁵. Structure III shows oxygen present only in the form of carbonyl groups. Evidence for this has been provided by model compounds, elemental analysis, infrared spectroscopy, mechanical properties and analysis of gases evolved during carbonization²⁷.

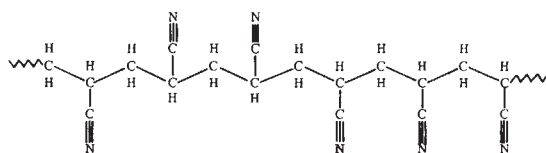
Structure IV shows each nitrogen atom donating its lone pair of electrons to an oxygen atom. This was proposed after

a study of model compounds⁹. The conclusions of this report are not consistent with any of these formulae.

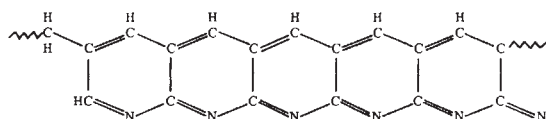
Two types of polymer fibres were used in this study—'Courtele' and polyacrylonitrile (homopolymer). 'Courtele' is stated to contain 6% methyl acrylate comonomer¹⁹. It may also contain about 1% of another vinyl monomer which acts as a dye site. Its stretch ratio is undeclared.

In contrast the polyacrylonitrile fibres were well characterized. Acrylonitrile was purified by distillation and polymerized using Redox free radical initiators to a conversion of 83%, and weight-average molecular weight of 220,000. The polymer contains acidic end groups and no attempt was made to fractionate. Fibres were spun from N-dimethylformamide solution using the wet spinning process with ethanediol coagulant. They were stretched eighteen times in two stages. Residual coagulant was evaporated off while the fibres were restrained on a frame.

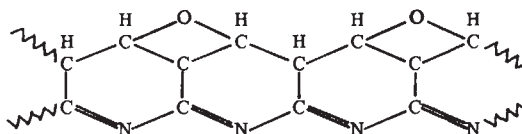
'Courtele' fibres have an approximately circular cross-



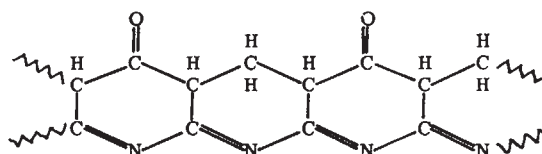
Ia



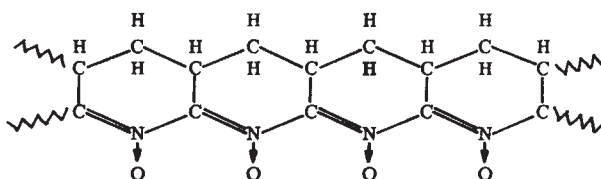
Ib



II



III



IV

section of diameter 13 μm , whereas the PAN fibres had a kidney-shaped cross-section of mean thickness 10 μm .

Films of both polymers (thickness approximately 12 μm) were prepared by solvent casting and were used in the infrared analysis.

For oxidation the fibres were restrained on a rectangular tube frame (4 inch long) in an air circulating oven at 225° C. For treatment in nitrogen the frames and films were placed in a 200 ml tube under a flow rate of approximately 100 ml min⁻¹ of nitrogen containing less than 0.1% oxygen.

A Perkin Elmer 420 Elemental Analyser was used to determine carbon, hydrogen and nitrogen contents: oxygen content was obtained by difference. Elemental analyses were carried out after various heat treatments and no account was taken of the escape of gaseous reaction products. It has been found that little weight change occurs during oxidation. Fiedler *et al.* showed that polyacrylonitrile fibres heated at 225° C for 5 h lose less than 2% overall weight¹⁷. This occurs while oxygen is being absorbed and water, hydrogen cyanide and ammonia are evolved. Watt has found that 3% of nitrogen is lost as hydrogen cyanide during the oxidation of copolymer fibres at 220° C (ref. 10). In the present work elemental contents are expressed in terms of the number of hydrogen, nitrogen or oxygen atoms per repeat unit, which contains three carbon atoms (Fig. 1).

The hydrogen content of 'Courtelles' precursor fibres is slightly greater than three atoms per monomer unit owing to the methyl acrylate comonomer. The loss of hydrogen is initially faster in 'Courtelles' than PAN, but after oxidation for 10 h the hydrogen content in both polymers is similar. The behaviour of nitrogen is nearly the same for both polymers and may be considered invariant. The oxygen content of 'Courtelles' is greater than zero owing to the methyl acrylate comonomer, and the slight oxygen content of PAN fibres may be a consequence of the acidic end groups. Measured by oxygen uptake, 'Courtelles' fibres initially oxidize faster than PAN fibres, but the oxygen contents after 10 h are very similar. The oxygen contents are better represented as the number of repeat units per oxygen atom (Fig. 2). When 'Courtelles' fibres are heated in nitrogen, there is no change in hydrogen, nitrogen or oxygen contents in the repeat unit (Fig. 1). These results indicate that, apart from differences in rates of reaction, there is little qualitative difference in the reactions between the two polymers.

After 5 h oxidation at 225° C, the repeat unit in 'Courtelles' should contain on average one hydrogen atom less, the same number of nitrogen atoms and one oxygen atom per two to three repeat units. After heat treatment for 5 h in nitrogen,

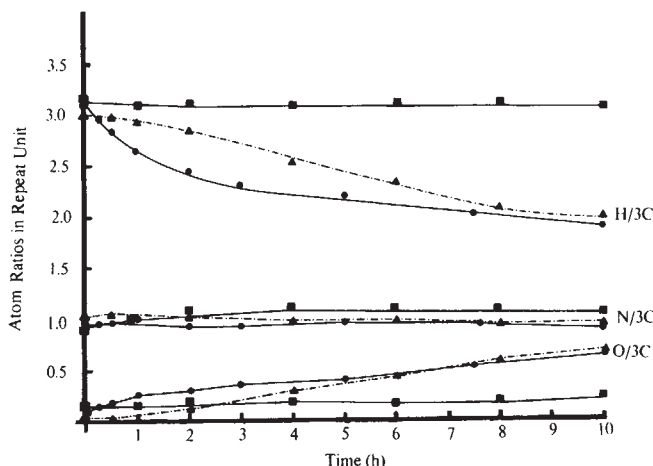


Fig. 1 Atomic ratios in repeat unit during thermal treatment (225° C) in air and nitrogen. Δ — Δ , Polyacrylonitrile fibres—air; $\bullet$ — $\bullet$, 'Courtelles' fibres—air; $\blacksquare$ — $\blacksquare$, 'Courtelles' fibres—nitrogen.

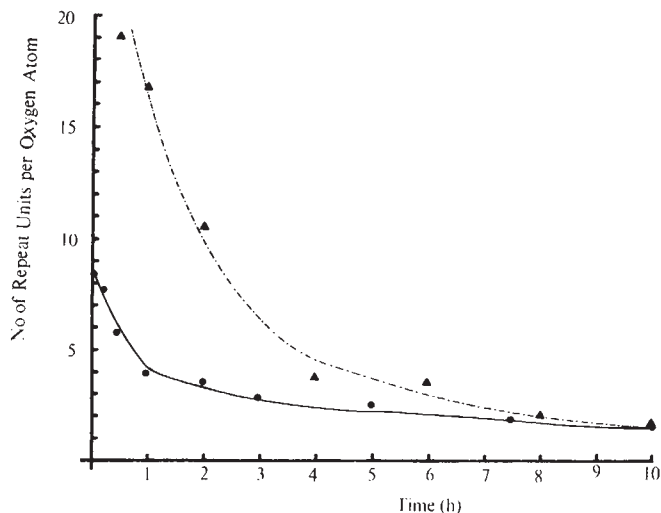


Fig. 2 Number of repeat units per oxygen atom during oxidation (225° C/air). Δ — Δ , Polyacrylonitrile fibres; $\bullet$ — $\bullet$, 'Courtelles' fibres.

the repeat unit should contain the same ratio of the elements as the precursor.

Qualitative Infrared Analysis

In the spectrum of polyacrylonitrile (Fig. 5a), the absorption peaks of particular interest are due to CH_2 (2,940 cm^{-1}) and $\text{C}\equiv\text{N}$ (2,240 cm^{-1}). The spectrum of 'Courtelles' (Fig. 3a) contains peaks additional to those in PAN; $\text{C}=\text{O}$ (1,730 cm^{-1}) and $\text{C}-\text{O}$ (1,170 cm^{-1}).

The spectra obtained from the fibres directly, using the KBr disk method were more satisfactory than those using the attenuated total reflectance method, although the spectrum between 4,000 cm^{-1} and 3,000 cm^{-1} was obscured because of a particle radiation scattering effect and residual moisture in the KBr.

When 'Courtelles' fibres are oxidized the reduction in intensities of peaks at 2,940 cm^{-1} and 2,240 cm^{-1} indicate that the CH_2 and $\text{C}\equiv\text{N}$ groups are reacting (Fig. 3). Also, new absorption peaks are created at 1,590 and 800 cm^{-1} and a shoulder forms at 2,180 cm^{-1} . After several hours of oxidation a broad absorption is created between 1,800 cm^{-1} and 1,000 cm^{-1} . With 'Courtelles' film (Fig. 4a) some changes also occur in the 3,400–3,000 cm^{-1} region. Otherwise the spectra taken of film and fibres are very similar.

The absorption at 2,180 cm^{-1} is probably caused by a nitrile group which is in electron resonance with another part of the molecule. In such circumstances it is a well known phenomenon that the frequency of vibration is decreased.

The absorption at 1,590 cm^{-1} may be assigned to $\text{C}=\text{C}$ and/or $\text{C}=\text{N}$ groups, and as it would have an important bearing on the formation of carbon fibres, this point is worth further discussion. If $\text{C}=\text{C}$ bonds are formed in this heat treated PAN system, only two types of substitution on the $\text{C}=\text{C}$ group are likely, $\text{R}_1\text{R}_2\text{C}=\text{CR}_3\text{R}_4$ and $\text{R}_1\text{R}_2\text{C}=\text{CHR}_3$, both of which would be expected to absorb between 1,675 cm^{-1} and 1,665 cm^{-1} (ref. 20). Conjugation and aromaticity, however, would be expected to shift the frequency of a particular absorption to perhaps 1,450 cm^{-1} . Another possibility is the formation of an $\text{R}_1\text{R}_2\text{C}=\text{C}=\text{N}-\text{R}_3$ group, but this is considered very unlikely. Similar $\text{X}=\text{Y}=\text{Z}$ systems have been found to absorb between 2,130 cm^{-1} and 1,900 cm^{-1} (ref. 25) where we found no absorption.

If the $\text{C}=\text{C}$ group carries a hydrogen atom, the $=\text{C}-\text{H}$ group would be expected to absorb in three regions because of the stretch, in-plane bend and out-of-plane bend vibrations. The stretch vibration would be expected to occur with medium intensity at 3,030 to 3,000 cm^{-1} whether the double bond was alkene or aromatic in nature. The in-plane bend vibration

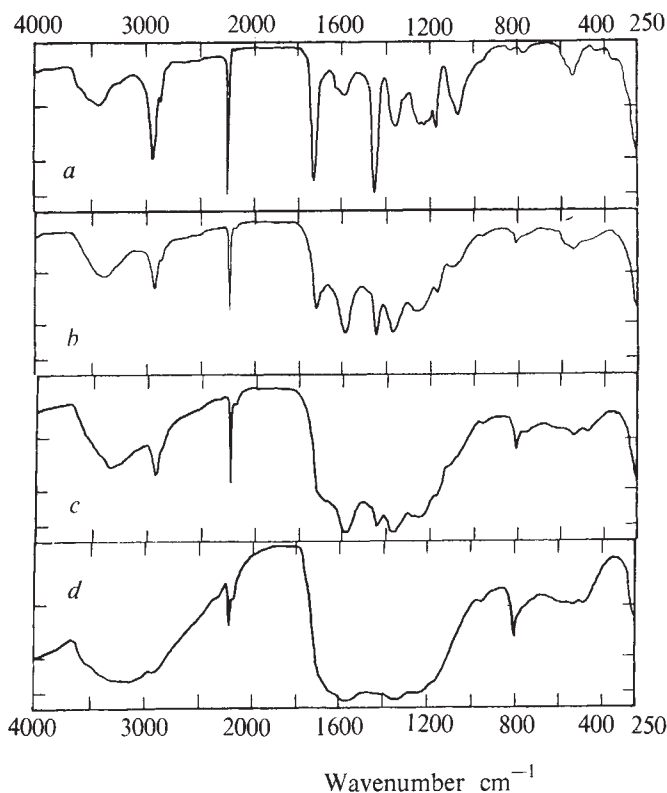


Fig. 3 'Courtelles' fibres heated in air at 225° C for *a*, zero; *b*, 0.25 h; *c*, 1.25 h; *d*, 5 h.

usually occurs at 1,450 to 1,250 cm^{-1} in alkenes and 1,250 to 1,000 cm^{-1} in aromatic molecules. The use of these absorptions in qualitative analysis of polymer systems is generally unreliable owing to their weak intensity and confusion through overlap with C—C and C—O stretching vibrations. Additionally, these vibrations can be confused with ring vibrations in 6-membered aromatic molecules, for instance pyridine derivatives absorb strongly at 1,250 to 1,000 cm^{-1} whereas the corresponding quinonoid molecules show no strong absorptions in this region²³. In this polymer system an alkene out-of-plane =C—H vibration would be expected to absorb strongly at 840 to 790 cm^{-1} whereas the corresponding vibration in an aromatic molecule may be found within a larger range 900 to 700 cm^{-1} .

In practice an intense absorption occurs at 1,590 cm^{-1} while a shoulder develops at 1,655 cm^{-1} . No significant absorption occurs at 3,030 to 3,000 cm^{-1} while an intense peak develops at 800 cm^{-1} . There seem to be no characteristic features on the absorption 1,550 to 1,000 cm^{-1} . So although there is evidence for the formation of carbon carbon unsaturation, a more intense absorption in the region 3,030 to 3,000 cm^{-1} at least, would have been expected.

At this stage additional information is provided by comparing the spectra of 'Courtelles' films which have been heated for similar periods in air and nitrogen (Fig. 4). It can be seen that whereas in the oxidized film peaks are produced at 3,330 cm^{-1} and 3,200 cm^{-1} , in the spectrum of the nitrogen treated film the peak at 3,330 cm^{-1} is reduced to a shoulder. This shoulder is further reduced in the corresponding spectrum of polyacrylonitrile film (not shown). Thus it seems that oxidation causes the formation of OH and NH groups whereas heat treatment in nitrogen produces NH groups and only small quantities of OH groups which probably originate from the oxygen in the copolymer molecules in 'Courtelles' and the end groups in polyacrylonitrile. The hydrogen required for the formation of NH groups when there is no oxidation must

come from degradation products, indicating that NH groups are formed at the ends of cyclized sequences.

Another important difference is the virtual absence in the spectrum of the nitrogen treated film of the peak at 800 cm^{-1} . This result is also reported elsewhere²⁴. Again this peak is reduced in the corresponding polyacrylonitrile film and is probably caused by oxygen in the polymer molecule. Thus it would seem that C=C groups are not formed to a significant extent when oxygen is absent and further evidence is provided by the retention of the CH₂ absorption at 2,940 cm^{-1} . But, equally important is that the 1,590 cm^{-1} is still present. This fact, together with the reduction in intensity of the nitrile peak (2,240 cm^{-1}) shows that C=N groups are being formed in the film heated in nitrogen. The nitrile peak, however, also decreases in the oxidized film so that it can be assumed that in this case also C=N groups are being formed. Further evidence is provided by the strong =C—H peak at 800 cm^{-1} which in the oxidized film develops much slower than the 1,590 cm^{-1} peak.

The formation of C=N groups is indicative of the development of heterocyclic structures. Other evidence is provided by thermal analysis⁸ and the observation, first described by Houtz⁴ that after heat treatment the polymer has greatly improved thermal stability.

The oxidation of polymers often results in the formation of carbonyl groups, but the spectrum of 'Courtelles' contains a strong carbonyl absorption from the comonomer. It can be seen from the spectra of PAN film during oxidation (Fig. 5) that carbonyl groups (1,710 cm^{-1}) are formed on oxidation. Apart from carbon carbon unsaturation, the shoulder at 1,650 cm^{-1} could be attributed to a carbonyl group in a β -diketene. Both these absorptions are absent in the spectrum of the polymer that was heat treated in nitrogen.

Previously, an empirical formula for the oxidized polymer was developed from the results of elemental and infrared analysis, and the assumption that oxygen was present only in the form of bridging ether groups¹⁵ (structure II). Although the present work does not allow us to comment on the possible formation of bridging ether groups, it has shown clearly that oxygen is present in the oxidized polymer in hydroxyl and carbonyl groups, and there is considerable evidence for the formation of fully aromatic heterocyclic structures; heat treatment in nitrogen leaves the carbon backbone chain relatively unaltered, however, whereas the heterocyclic structures are still formed with conjugation between the C=N groups.

It is desirable to take quantitative measurements for the fibres from their spectra. This is not possible owing to the uncertainty of equating, between the KBr disks, the amount of material which is absorbing radiation. It is, however,

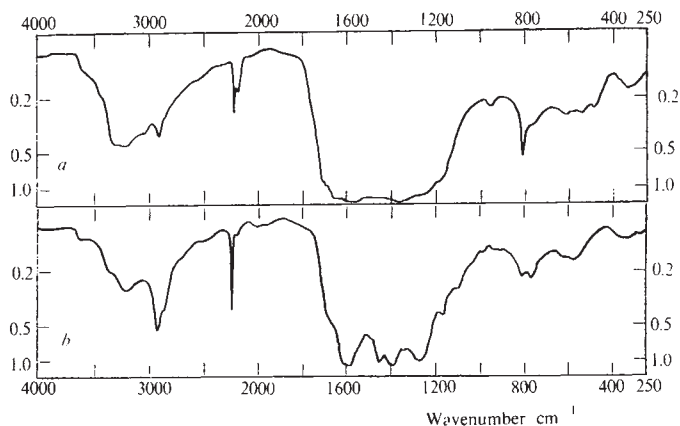


Fig. 4 'Courtelles' film heated at 225° C for 9 h in *a*, air; *b*, nitrogen.

possible using film provided the assumption is made that the thickness of the film does not change during the treatment.

In order to use the measurements made on the film to give information about the fibres, a parameter has to be used which is independent of the absorption characteristics of the particular form of the specimen. For both fibres and film, graphs are drawn of the change of this parameter with heating time. Then, for any particular value of the parameter, the fibres and film are said to be equivalent at their corresponding heating periods as found from the graphs.

The parameter which has been used for 'Courtele' fibres and film is the ratio of intensities of absorptions at $2,180\text{ cm}^{-1}$ and $2,240\text{ cm}^{-1}$ (Fig. 6). These have been chosen because their baselines are most easily determined. 'Courtele' fibres which have been oxidized for 5 h at 225°C in air are found to be equivalent to the film which had had 8 h oxidation. In this film, and therefore in the fibres oxidized for 5 h, five out of seven of the original nitrile groups had "reacted". In this

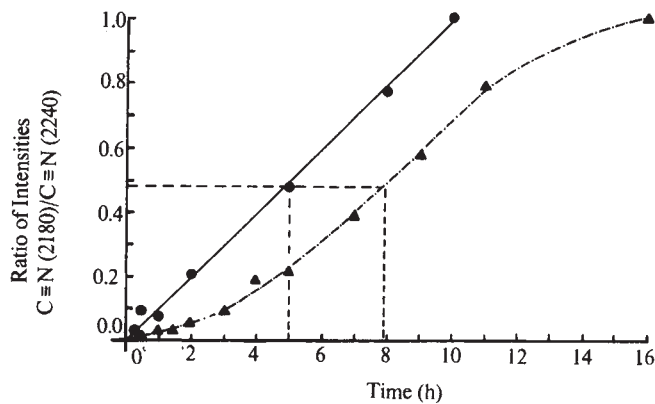


Fig. 6 Correlation between 'Courtele' fibres and film during oxidation at 225°C in air. ●, Fibres; ▲, films.

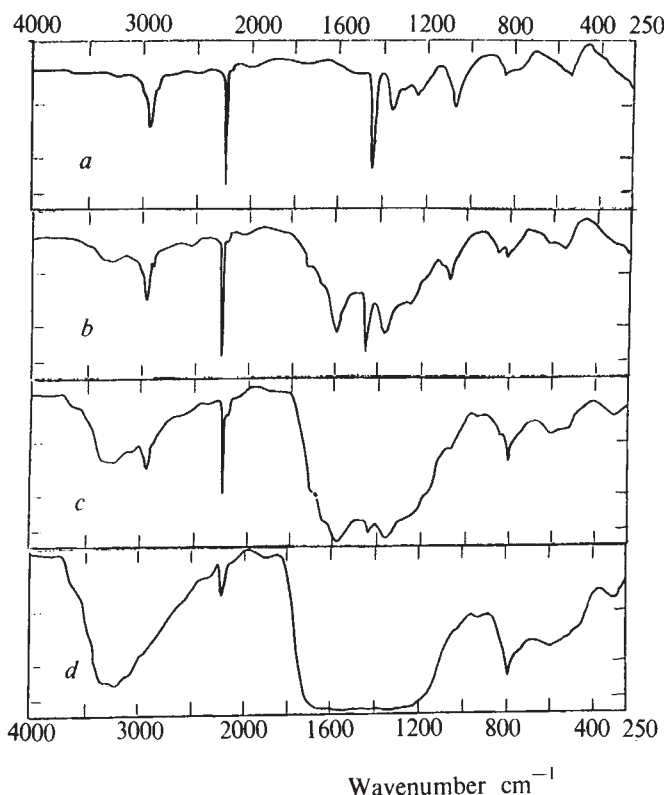


Fig. 5 Polyacrylonitrile film heated in air at 225°C for a, zero; b, 4 h; c, 10 h.

sense "reacted" means either to have become conjugated or have actually reacted to a $\text{C}=\text{N}$ group.

Using the same method for 'Courtele' fibres and film which had been heated in nitrogen, it was found that in fibres which had been heated for 5 h, one out of two of the original nitrile groups has "reacted".

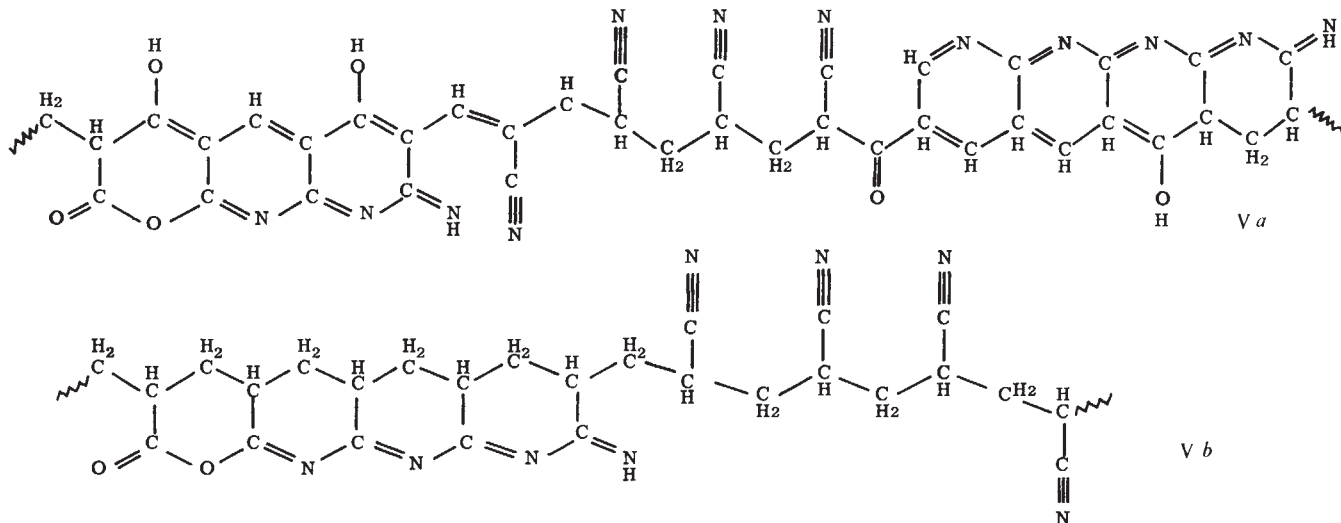
Unfortunately, no method has been found for accurately measuring the length of the cyclized sequences, using infrared spectroscopy.

Chemical Formulae for the Heat-treated Polymer

We are interested, not in the formula of the fully oxidized polymer, but of 'Courtele' fibres which have been heated at 225°C in air for 5 h. In these conditions both elemental analysis and infrared spectroscopy indicate that only partial oxidation has been achieved.

The following quantitative parameters have been determined: the ratios hydrogen, nitrogen and oxygen to carbon, and the ratio of the number of the original type of nitrile groups remaining to the number that have "reacted". These parameters have been incorporated in the proposed chemical formulae of both oxidized Va and non-oxidized fibres Vb. Otherwise these formulae are merely a possible collection of the chemical species shown to be present, and no inference may be made regarding the order of the groups. Also hydrogen bonding possibilities have been omitted for clarity, but it is likely that both inter and intramolecular hydrogen bonding is present.

It has been shown that comonomers containing carboxylic



groups can initiate the cyclization reactions¹³, and this feature is included in the formulae.

Implications

When 'Courtelles' fibres are heated in air, two basic types of reaction occur, oxidation and cyclization. Cyclization also occurs in fibres which have been heated in an inert atmosphere.

By comparison with the cyclized sequences in the nitrogen treated polymer, those in the oxidized polymer are stiffer and more thermally stable because they are aromatic and have greater bond energies. The oxygen in the oxidized polymer is present as hydroxyl groups, which are substituted into the main chain probably in β positions, and carbonyl groups.

The morphology of the oxidized molecule can be considered to be stiff, planar cyclized rings connected by relatively mobile linear segments. Different cyclized sections will be in different planes. When the molecule is heated in the early stages of carbonization, the linear segments will twist allowing different cyclized sequences to become planar, so laying the foundations of the graphite structure. The driving force for this alignment could be a condensation reaction between the hydroxyl groups: water has been analysed in the evolved gases at early stages of carbonization^{6,17}.

It would seem that oxidation is necessary for at least two reasons. It allows the formation of conjugated and aromatic structures which are more capable of withstanding the temperatures of carbonization without molecular breakdown. Crosslinking through condensation reactions in the early stages of carbonization further stabilizes the structure. If oxidation is omitted the cyclized segments are not aromatic: only the C=N groups are conjugated. Thus the bond energies in the ring will be lower, allowing more possibility of chain scission. The absence of hydroxyl groups may result in the non-alignment of different cyclized sequences. Both effects will allow a relatively disordered structure to develop, and the formation and retention of molecular orientation, referred to at the beginning, will have been lost.

We can consider the oxidized fibre as the precursor fibre, and use it as a model for other precursor fibres. We can say that in general the precursor fibre must be thermally stable. This means we must build into the polymer molecule electron delocalization and aromaticity. But these are the very properties which must be excluded in order to be able to stretch the

fibre and produce a high degree of molecular orientation. We suspect therefore that it will not be possible directly and easily to produce a carbon fibre with good mechanical properties from thermally stable polymers. We must resort to producing a linear plastic polymer with poor thermal stability, which can easily be softened and stretched to produce the required molecular alignment. Then we must carry out a chemical reaction to convert the polymer molecules into cyclic aromatic structures without loss of molecular orientation.

We thank Dr B. C. Stace for his advice and assistance.

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Double Helix at Atomic Resolution

JOHN M. ROSENBERG, NADRIAN C. SEEMAN,
JUNG JA PARK KIM, F. L. SUDDATH,
HUGH B. NICHOLAS* & ALEXANDER RICH

Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

The sodium salt of the dinucleoside phosphate adenosyl-3',5'-uridine phosphate crystallizes in the form of a right handed antiparallel double helix with Watson-Crick hydrogen bonding between uracil and adenine. A sodium ion is located in the minor groove of the helix complexed to both uracil rings.

MANY important functions in molecular biology are determined by antiparallel double helical nucleic acids with complementary base pairing between the two strands, as first described by Watson and Crick¹. Although considerable work has been carried out on the structures of double helical nucleic acids²⁻⁸, the fine details of their molecular architecture have never been available at atomic resolution. The X-ray diffraction patterns shown by fibres of DNA and RNA characteristically die out at resolution greater than about 3 Å. Because of this, there has been considerable discussion⁹⁻¹³ about the actual nature of the detailed stereochemistry and hydrogen bonding in double

helical DNA. One way to obtain additional information about these atomic details is to crystallize oligonucleotide fragments of known sequence which may form double helices in the crystal lattice. Here we report the single crystal X-ray analysis of the sodium salt of adenosyl-3',5'-uridine phosphate (ApU) which forms a right handed antiparallel double helix in which the ribose phosphate backbones are held together by Watson-Crick hydrogen bonding between the adenine and uracil residues. This is the first crystal structure in which the atomic details of double helical nucleic acids can be visualized. In addition, this is the first single crystal structure showing Watson-Crick base pairing between adenine and uracil.

Experiments

The sodium salt of ApU (Miles) was mixed stoichiometrically with bromotertiary butyl amine in a 40% solution of 2-methyl-2,4-pentanediol (MPD). A small volume of the solution was placed in equilibrium with a large reservoir of 60% MPD in a closed container which was stored at 4° C. After standing for 2 weeks, small prismatic crystals with well defined faces began to appear. Crystal growth continued slowly for several months and yielded crystals suitable for X-ray analysis. The amine was put into the solution in the hope that it might become the cation of the structure; however, subsequent analysis revealed that the sodium salt had crystallized rather than the bromoamine. A crystal measuring 0.2 mm × 0.15 mm × 0.05 mm was mounted on the tip of a glass fibre for X-ray analysis. The crystal was found to be monoclinic, space group $P2_1$, with cell dimensions $a=18.025$ Å, $b=17.501$ Å, $c=9.677$ Å, $\beta=99.45^\circ$. The crystal density measured in a density gradient was 1.53. In order to obtain a calculated density near the observed density, it was necessary to assume four molecules of Na^+ApU^- and twenty-two water molecules in the unit cell. This surprisingly high degree of hydration was subsequently shown to be a low estimate as solution of the structure revealed twenty-four water molecules in the unit cell. Three-dimensional X-ray diffraction intensity data were collected out to a resolution of 0.8 Å, with a 'Picker' FACS-1 diffractometer in an 'Omega' step scan mode, using Nickel filtered $\text{CuK}\alpha$ radiation. The data were collected at 8° C and were corrected for Lorentz and polarization effects; no absorption correction has been applied because of the low mass absorption coefficient (18.0).

Solution of the Structure

Although there was no crystallographic two-fold axis in the lattice, the presence of a peak nearly 40% the height of the origin on the Harker section of the Patterson function suggested a non-crystallographic two-fold axis in the structure. From this we inferred the double helical nature of ApU. This peak was assumed to contain all vectors from each atom of one ApU molecule to the corresponding atom of the other independent molecule, symmetry related. From previous work with the protonated dinucleoside phosphate uridyl-3',5'-adenosine phosphate¹⁴ (UpA), it was known that resolution difference Patterson techniques were effective in discriminating vectors arising from two second row atoms in a large structure. (Resolution difference Patterson techniques are those in which two Patterson or superposition functions, for example, multiple minimum functions or N -atom symmetry minimum functions are compared. These two Pattersons are (1) the standard F^2 Patterson, calculated using all the diffraction data, and (2) a Patterson calculated only from the higher order reflexions whose F s should contain a larger contribution from the heavier atoms sought as they are relatively denser near the atomic centres. The origins of both Pattersons are normalized to the same value. Peaks arising from heavy atom-heavy atom vectors ought to be relatively more prominent than overlapping light atom-

light atom vectors in the second map. In this work, the first Patterson contained all the 1 Å data, and the second function contained the data in the shell between 1.5 Å and 1 Å.)

UpA contained seventy-seven first row atoms. Thus, we hoped to locate the phosphorus atoms by using this vector as the basis vector of a Resolution Difference 2-Atom Symmetry Minimum Function^{15,16} (RDSMF(2)). The RDSMF(2) initially indicated the wrong location for the phosphorus atoms, however, which was obvious when Fourier refinement procedures failed to reveal the structure. An (E^2-1) Patterson (E is the quasinormalized structure factor) was therefore calculated and the map and its Fourier coefficients were corrected for non-negativity and minimal bond lengths according to the procedure proposed by Karle and Hauptman¹⁷: (1) all negative points in the Patterson map and all points within a 0.9 Å radius of the origin were zeroed; (2) the map was Fourier transformed and all resultant (E^2-1) coefficients less than -1 were raised to -1 ; (3) a new Patterson map was calculated from these coefficients, and the process was iterated until convergence was obtained at forty cycles. From the final amplitudes, a set of thermally sharpened F s were generated, and used to calculate Patterson functions. The RDSMF(2) calculated from these Pattersons revealed the proper phosphorus locations. Approximate phosphate orientations were derived from Patterson superpositions. Fourteen cycles of Fourier refinement using the corrected E s as Fourier amplitudes revealed the two molecules of ApU, the sodium ions and four water molecules. The other water molecules were located in a series of difference syntheses. The structure has been refined using isotropic thermal parameters and only the 1 Å observed data by full matrix least squares. The current R factor is 0.091. (The discrepancy factor, R , is defined as $R = \sum |F_o| - |F_c| / \sum |F_o|$, where $|F_o|$ and $|F_c|$ are the amplitudes of the observed and calculated structure factors, respectively.) Because this is one of the larger non-centrosymmetric biological crystal structures solved without isomorphous replacement, we will expand on the details of the solution in a later publication.

Structure

In the analysis of this structure, there are two striking features. The non-crystallographic pseudo two-fold axis mentioned above rotates one ApU molecule into the other, so that the structure forms a segment of a right handed antiparallel double helix in which the bases are hydrogen bonded to each other in the Watson-Crick manner, as shown in Figs. 1 and 2. This is the familiar hydrogen bonding between adenine and uracil which is believed to occur quite generally in double helical nucleic acids. Nonetheless, this type of hydrogen bonding had never been seen previously in single crystal X-ray analysis. It should be noted that the two-fold axis to which we are referring lies half-way between the base planes, rather than in those planes. Axes in the planes are the ones usually discussed in the literature, but the periodic nature of double helices generates symmetry elements at both locations.

The other prominent feature was that the crystal was heavily hydrated, so that the ApU molecules are surrounded by large numbers of water molecules. This observation, coupled with the non-crystallographic nature of the two-fold axis, leads us to believe that the double helical nature of ApU is a function of the molecules themselves, rather than crystal packing forces.

The separation between the base pairs is 3.4 Å and, as can be seen in Fig. 1, there is a considerable degree of stacking in the structure. The $\text{NH} \dots \text{O}$ hydrogen bonds between the N6 amino group of adenine and the O4 carbonyl oxygen of uracil (see Fig. 3 for the numbering scheme) have bond lengths of 2.95 Å and 2.91 Å. The $\text{NH} \dots \text{N}$ hydrogen bonds between uracil N3 and adenine

N1 have lengths of 2.82 Å and 2.86 Å. The important distances across the base pairs between the two ribose carbon atoms C1' of the glycosidic linkage, are 10.50 Å and 10.53 Å. Similar distances to these have been obtained by analysis of single crystals of intermolecular complexes of purine and pyrimidine derivatives¹⁸ but this is the first time that these distances have been observed in a molecule which forms a fragment of a double helix.

The helical form of the molecules can be seen in Fig. 1 in which one is looking in a direction perpendicular to the base pair plane. There is clearly a rotational relationship between the glycosidic bonds (C1' to adenine N9 or C1' to uracil N1) of the front and rear base pairs. Another view of the structure parallel to the stacked hydrogen bonded bases is shown in Fig. 2. The right handed helical rotation can readily be seen by observing the orientations of adjoining ribose residues on the ribose phosphate chain. This structure is similar to that which has been deduced from studying double stranded viral RNA. The naturally occurring material is called RNA 11. Fig. 2 shows similar

In the protonated structure UpA, it was noted that there were short distances between adenosine C8 and O5', as well as uridine C6 and O5' (ref. 14). At that time, it was suggested that this might be a result of an intramolecular attraction which, if of a general nature, would help stabilize the anticonformation of the nucleotide. Accordingly, the related distances in this structure were examined with great interest. Three of the four independent distances were greater than or equal to 3.3 Å; thus, there was no evidence of any interaction. But the distance between one adenine C8 and its ribose O5' was 3.07 Å. As this O5' is not covalently linked to a phosphorus atom, the phenomenon may not be relevant to the nucleotides in a helical polynucleotide chain. Nevertheless, for non-helical and 3' terminal nucleic acid structures, this interaction may yet be seen to play an important role.

The individual double helical fragments are separated in the crystal lattice by a spacing of 3.4 Å, with considerable overlapping of the adenine residues. Besides this intermolecular base stacking, the other important interaction in

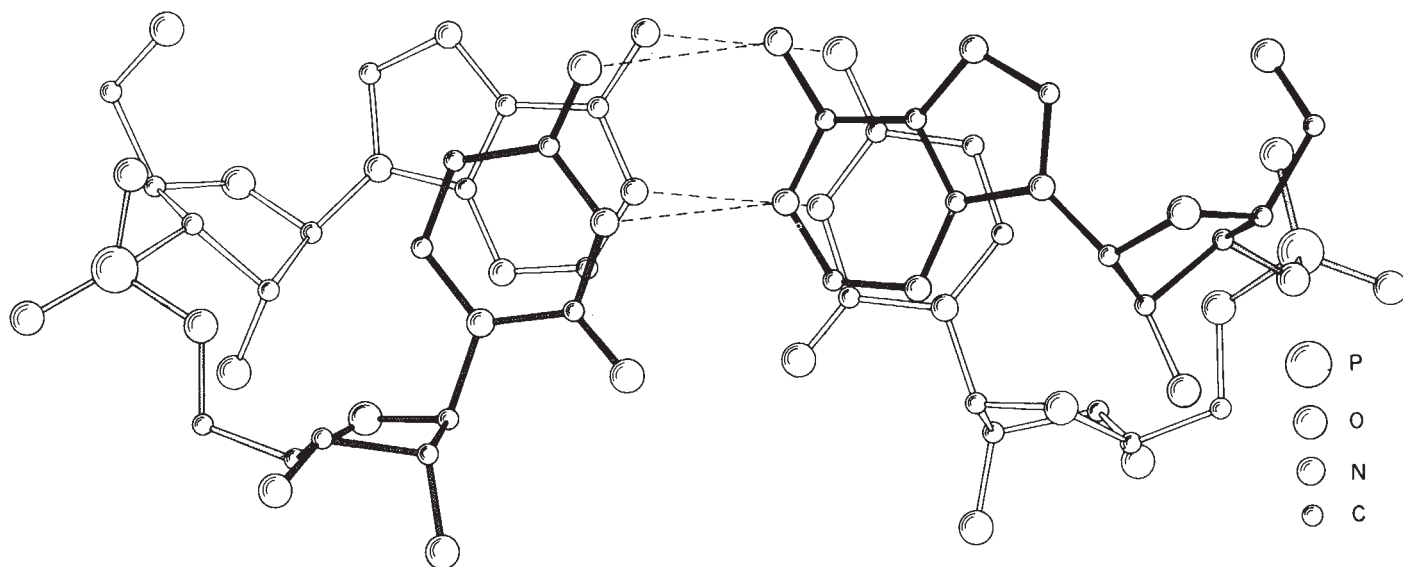


Fig. 1 View of the crystal structure perpendicular to the base planes showing hydrogen bonding (dashed lines) as well as the base stacking interactions. The darkest portions of the figure are those nearest the viewer. The rotational relationship is easily seen by comparing the front (black) and rear (white) glycosidic bonds.

views of ApU and RNA 11, where the dashed vertical line represents the approximate helix axis. The continued extension of the ApU nucleotide pairs would generate a right handed double stranded helix similar to RNA 11. It is important to note that although the helical parameters of RNA 11 can be derived directly from an X-ray analysis of the fibre, the positions of the atomic centres are of necessity inferred from data derived from single crystal studies of small molecules rather than from direct observation.

Although the two molecules of ApU in the asymmetric unit are very similar, they are not quite identical. The bond lengths and angles are all within expected range. The conformations of the ribose residues are all 3'-endo¹⁹, and the nucleosides are orientated in the anticonformation²⁰, with torsion angles about the glycosidic bonds¹⁹ of 2° and 7° for the adenosine residues, and 29° and 30° for the uridines. Comparison with the protonated UpA structure^{21,22} suggests that discrepancies between adenine and uracil torsion angles are caused by the differences between the 3' and 5' ends of the molecule as the same pattern was obtained with respect to the 3' and 5' ends in that molecule which had the opposite base sequence.

the direction perpendicular to the base pairs involves the proximity of O1' of both adenosine riboses with uracil rings. A similar type of interaction was found to be important in the crystal structure of UpA^{21,22}.

The crystal structure can be visualized as a rod-like entity. The central portions of these rods contain the stacked base pairs. These are flanked by the ribose phosphate backbones, both of which in turn are surrounded by the solvent structure. The large amount of water allows the crystal structure to assume a conformation which is minimally perturbed by lattice interactions. Thus, the double helical structure which we observe here bears a marked resemblance to those structures proposed for solvated polynucleotides. It should be noted in passing, however, that the water is held rather firmly, as the intensity data were collected from the crystal while it was mounted in air.

The ribose phosphate chains are packed together with the phosphate groups facing each other. In the layer between the ribose phosphate moieties are sodium ions which are found in two distinct sites: one, complexed between phosphate groups, and the other, surprisingly, bound to the uracil residues. The sodium ions and their ligands are

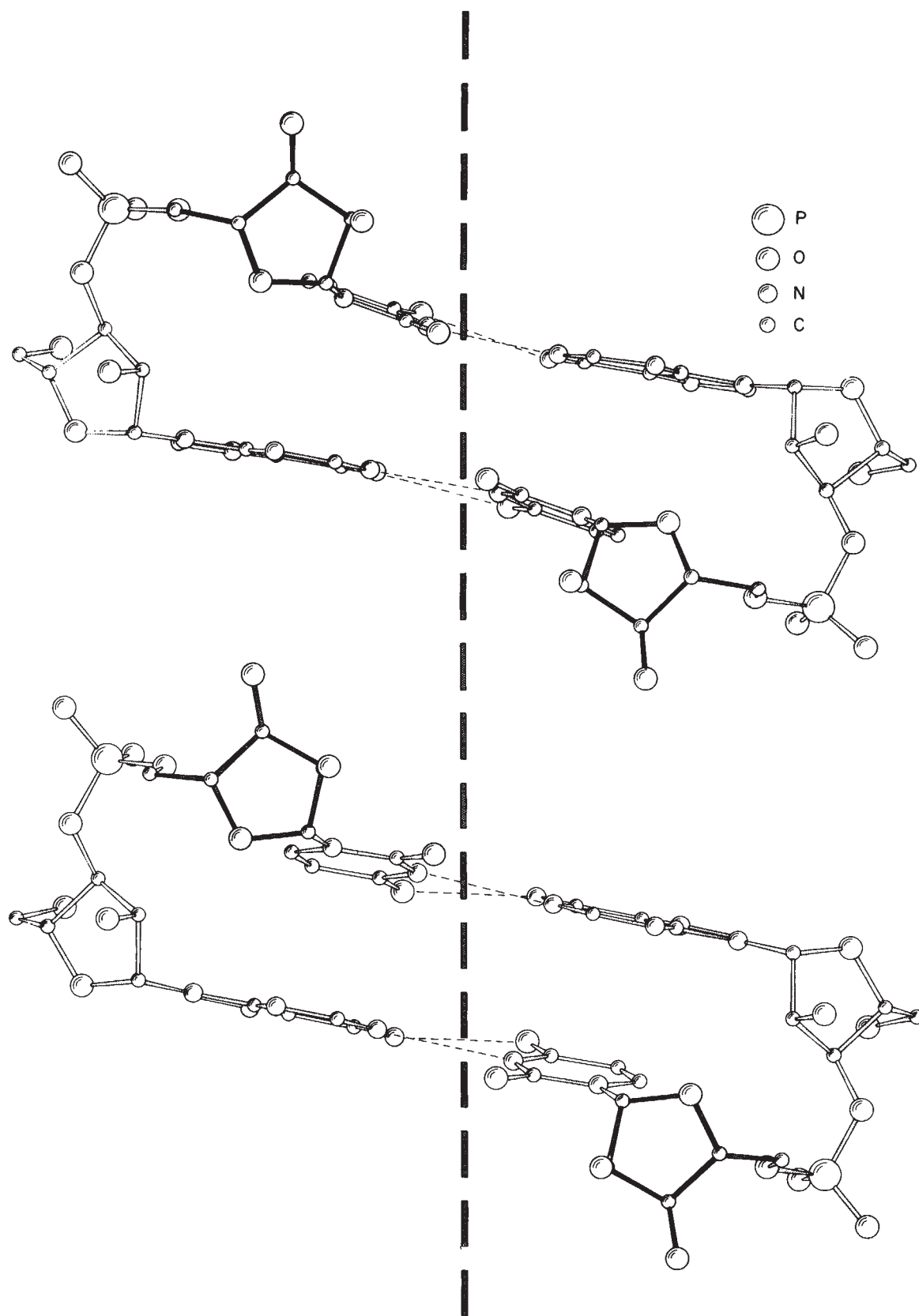


Fig. 2 Comparison of the structures of ApU (upper) and RNA 11 (lower). This view is approximately perpendicular to the helix axis which is indicated by the vertical dashed line.

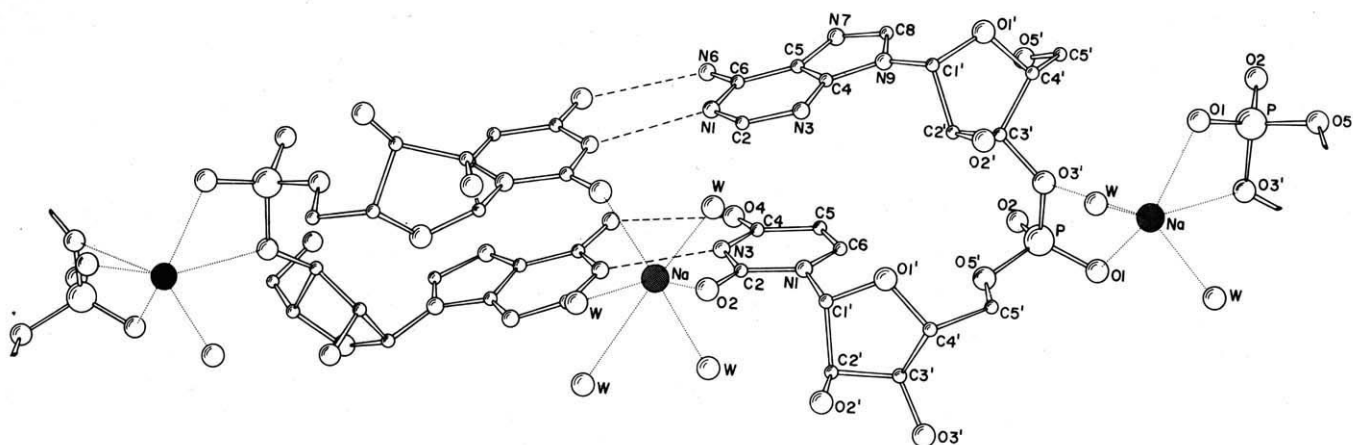


Fig. 3 Perspective view of the structure as seen from the minor groove showing the numbering scheme and the coordination of the sodium ions. Both sodium ions have distorted octahedral coordination involving water molecules (●) and other oxygens. The central sodium ion is 2.36 Å from the uracil O2 atoms.

shown in Fig. 3. The sodium ion in the centre is located on the pseudo two-fold axis in the minor groove of the helix with octahedral coordination which includes the free O2 atoms of the uracils; the remaining ligands are water molecules. As shown in Fig. 3, the other sodium ion rests on an intermolecular pseudo-dyad axis, also exhibiting octahedral coordination, which includes two adenosyl O3' atoms and two phosphate oxygen atoms.

The stability of the sodium ion position between two phosphate groups is readily understood on electrostatic grounds. What is not so obvious is why the second sodium ion is complexed to the two uracils in the minor groove of the helix. Five angstroms away from this site there is another position between two phosphate groups which could comfortably accommodate the sodium ion and is occupied only by solvent. It is possible that the structure is stabilized considerably by the sodium ion in the minor groove site. Should this prove to be of more general occurrence in other crystals containing A-U sequences, it is possible that this type of coordination may be of importance in polynucleotide structure and function.

As noted above, one of the most significant features of the organization of the crystal structure of ApU is that the two independent molecules in the asymmetric unit have very similar but not quite identical conformations. Thus, they are related by a pseudo two-fold rotation axis while in an antiparallel double helical polynucleotide there is presumed to be a true two-fold axis which relates the backbones of the two antiparallel chains. We do not completely understand why the crystal structure of ApU did not adopt a true two-fold axis. In this regard, however, we recently discovered that the closely related dinucleoside phosphate, guanosyl-3',5'-cytidyl phosphate does indeed form a right handed antiparallel double helix in the crystalline state in which this two-fold axis is crystallographic (unpublished results of R. O. Day, N. C. Seeman, J. M. R., and A. R.). This recent observation lends support to our earlier emphasis on the importance of the pseudo two-fold axis in the present crystal structure.

Among the significant facts which we learn by analysing double helical fragments are the important detailed parameters determining the conformation of the polynucleotide chain, especially those parts dealing with the geometry of the phosphate group. The structure of the ribose phosphate chain is of central importance in understanding the physical properties and behaviour of polynucleotide chains²³. This information should prove valuable in interpreting the details of the molecular structure in polynucleotide double

helices, as well as in the more complex forms of RNA such as those observed in tRNA²⁴.

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* Present address: Biophysics Laboratory, University of Wisconsin, Madison, Wisconsin 53706.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Anomalous Helium Abundance of the Galactic Centre HII Region G0.5-0.0

WE report here a search for the $\text{He}109\alpha$ line from the galactic centre HII region G0.5-0.0. Our failure to detect the line sets an upper limit to the abundance of helium which is about 10% of the abundance found in many HII regions. Our limit of 0.01 for the abundance of helium relative to hydrogen is even lower than the limits of 0.021 and 0.025 recently reported¹ for two other galactic centre regions, G0.7-0.0 (Sgr B2) and G0.2-0.0.

Observations of the 109α radio recombination lines of hydrogen and helium were carried out in October 1972 using the Parkes 64-m radio telescope, which has a beam-width of 4.1 arc min at this frequency (5 GHz). The receiving system had an overall noise temperature of 80 K and was followed by a bank of contiguous filters with 100 kHz bandwidth² to give an equivalent velocity resolution of 6 km s⁻¹. A digital computer controlled the receiver, switching between the antenna feed and a cooled reference termination, calibrating the system at frequent intervals, and collecting, processing and displaying the data as a sixty-four-point spectrum.

Fig. 1 shows the spectrum of G0.5-0.0 derived by averaging observations totalling 15 h on source. Each observation measured the difference spectrum between the source and a region of blank sky observed over the same zenith and azimuth range. The beam brightness temperature scale was established by observing Hydra A, for which a flux density of 13.50 f.u. was assumed. The velocity scale is for $\text{H}109\alpha$ relative to the local standard of rest. The $\text{H}109\alpha$ line in G0.5-0.0 consists of an intense component and two low intensity components, indicating at least three HII regions in the line of sight. No significant peak is seen at the frequency of the $\text{He}109\alpha$ line.

With the assumption of low optical depth in the continuum and the line, observations of a pair of $\text{H}\alpha$ and $\text{He}\alpha$ lines yield the ratio of a weighted average of the number of helium atoms in the upper excitation state to the corresponding average for hydrogen atoms in the nebula. This ratio gives the total number abundance of helium to hydrogen using the assumptions that: the helium and hydrogen have the same distribution throughout the nebula; the line enhancement factors and the deviations from LTE populations are the same for both helium and hydrogen; the helium and hydrogen are ionized in the same volume of space; and there is no doubly ionized helium.

With these assumptions, and assuming equal widths for the hydrogen and helium lines (measurement of $\text{H}109\alpha$ and $\text{He}109\alpha$ lines in twenty southern HII regions yield a mean value for the ratio of the line widths of hydrogen to helium of 1.05 ± 0.16 r.m.s. (unpublished results from Churchwell and Huchtmeier⁸ and our work) and an intensity limit of three times the r.m.s. noise, our observations place an upper limit on the number abundance of singly ionized helium (plus heavier elements) of 0.01. This is considerably lower than the previous limit of 0.041 for this source³.

Our first two assumptions seem to be satisfied in all HII regions and have been discussed in other places (see for

example Palmer *et al.*⁴). The other two assumptions are satisfied to varying degrees in different HII regions and will be considered in turn for G0.5-0.0.

For exciting stars of spectral type earlier than about O7, calculations by Rubin⁵ have shown that in an HII region of uniform density the Strömgren radii of HeII and HII will be essentially equal. If, however, high density condensations occur within the ionized hydrogen region there will be volumes (shadow zones) where helium is not ionized^{6,7}. For Orion A, M8 and M17, in which such condensations occur^{8,9} the optical observations of Peimbert and Costero¹⁰ show the abundance of neutral helium to be between 0.01 and 0.03 relative to ionized hydrogen. This is less than one-third of the total helium abundance; if a similar ratio applies for the HII region G0.5-0.0 the presence of condensations will not greatly affect our upper limit. If, on the other hand, the exciting star is of a spectral type later than O9.5 the radius of the HeII region will be considerably smaller than that of the HII region and an appreciable amount of the helium is left unionized. Such a case seems to occur in the HII region NGC 2024 for which the excitation parameter is small ($u=27$ cm⁻² pc) and for which the exciting star has been identified as being of spectral type B0.5. For this HII region the upper limit to the singly ionized helium abundance is 0.02 (ref. 4). The present source, G0.5-0.0, has a relatively high excitation parameter (237 cm⁻² pc; see Table 1) by comparison with other galactic HII regions for which recombination line observations show "normal" helium abundance. Its emission measure, electron density and ionized mass (Table 1) are well within the range of values for other HII regions so it is likely that most of its helium is ionized.

The possibility that an important percentage of the helium is doubly ionized has to be considered. For both Orion A and M17, radio recombination line measurements⁴ and optical measurements (Peimbert, see ref. 11) have established an upper limit of 10^{-3} for the number abundance

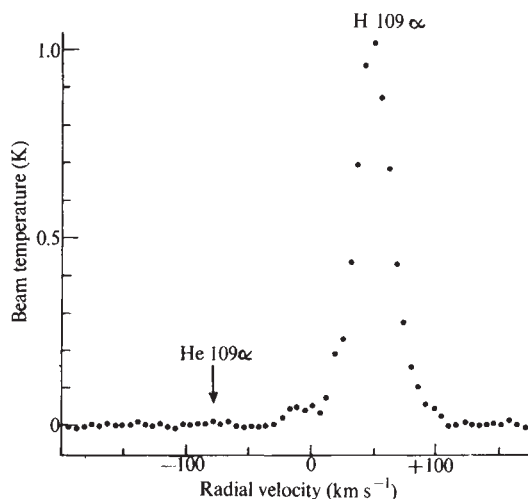


Fig. 1 The $\text{H}109\alpha$ recombination line in the galactic centre source G0.5-0.0 is displayed as full-beam brightness temperature against radial velocity of $\text{H}109\alpha$ relative to the local standard of rest. The expected frequency of any corresponding $\text{He}109\alpha$ line is indicated by an arrow.

Table 1 Measured Parameters of the HII Region G0.5-0.0

Radio continuum flux at 5 GHz	38.3 f.u.
Full-beam brightness temperature:	
Continuum peak	14.2 K
H109 α line peak	1.03 K
H109 α radial velocity (l.s.r.):	
Principal feature	$+47.4 \pm 1.2$ km s $^{-1}$
Low intensity features	-13.0 ± 3.0 km s $^{-1}$ $+88.9 \pm 3.0$ km s $^{-1}$
H109 α line width (corrected for filter broadening)	556 ± 20 kHz
N(HeII)/N(HII)	< 0.01
Derived parameters*	
Electron temperature (L.T.E. condition), T_e	$5,500 \pm 800$ K
Emission measure, E	2.5×10^5 cm $^{-6}$ pc
Electron density, N_e	103 cm $^{-3}$
Ionized mass, $M_\odot$	1.1×10^4
Excitation parameter, u	237 cm $^{-2}$ pc

* Derived on the assumption of a spherical model HII region.

of doubly ionized helium relative to ionized hydrogen. Martin and Downes¹² found that potential external sources of ionization were too inefficient to ionize helium doubly in G0.7-0.0. It therefore seems reasonable to assume that the amount of doubly ionized helium in G0.5-0.0 is negligible. (For G0.2-0.0 and G0.7-0.0 radio observations¹ established an upper limit for doubly ionized helium of 0.01. Adopting a similar limit for G0.5-0.0 would raise our limit for the singly and doubly ionized helium abundance from 0.01 to 0.02.)

Most astronomical objects, galactic and extra-galactic HII regions, O and B stars, planetary nebulae, solar chromosphere and prominences, and solar cosmic rays have helium abundances between 0.07 to 0.14. Stellar evolution models also require values in this range to match the observed characteristics of stars. Thus from the foregoing discussion it seems that the galactic centre HII regions are deficient in helium—a characteristic they share with many halo Bp stars^{13,14} and some QSOs.

Generation of helium within main sequence stars can account for a number abundance of only 0.01 (ref. 15). An alternative hypothesis that helium originated in galactic nuclei ("little bang", see, for example, Burbidge and Burbidge¹⁶) certainly finds no support from these observations, which show a deficiency near the galactic nucleus. Another possibility is that helium originated in the early stages of the Universe. Independent computations by two groups¹⁷⁻²⁰ have indicated that a number abundance of about 0.1 could be produced in the universal fireball. On the other hand, a number of authors (see, for example, refs. 20 and 21) have discussed phenomena which might have produced an amount of primordial helium of 0.01 or lower. So far no theory simultaneously accounts for a helium abundance of about 0.1 in most astronomical objects and helium-deficient regions such as G0.5-0.0.

W. K. HUCHTMEIER
R. A. BATCHELOR

Division of Radiophysics, CSIRO,
Sydney

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Physical Background of the Geoidal Figure

R. R. ALLEN has recently considered the depth within the Earth of the origins of the gravitational anomalies, and other studies have been reviewed in *Nature*¹. Plainly the time has now come when enough is known about the characteristics of the geoid to make possible a definition of density variations within the Earth.

Table 1 Approximation of the Equatorial Section of the Geoid by Two Zonal Spherical Harmonics of Fifth Degree (Σ_1, Σ_2) from the Directions 58° resp. 156.5°

λ (°)	Σ_1 (m)	Σ_2 (m)	$\Sigma_1 + \Sigma_2$ computed (m)	Measured (m)	Δ Measured-computed (m)
58	-26.4	-37.3	-63.7	-58.7	+5.0
68	-26.6	-53.5	-80.1	-80.5	-0.4
78	-25.9	-58.4	-84.3	-92.5	-8.2
88	-20.9	-48.5	-69.4	-76.8	-7.4
98	-8.2	-27.6	-35.8	-33.0	+2.8
108	+5.6	-1.4	+4.2	+16.3	+12.1
118	+19.4	+23.6	+43.0	+47.8	+4.8
128	+25.0	+43.2	+68.2	+59.8	-8.4
138	+19.4	+55.4	+74.8	+64.8	-10.0
148	+4.6	+61.4	+66.0	+67.7	+1.7
158	-12.3	+63.0	+50.7	+61.2	+10.5
168	-23.3	+60.0	+36.7	+43.3	+6.6
178	-23.8	+53.2	+29.4	+25.4	-4.0
188	-14.1	+39.0	+24.9	+17.7	-7.2
198	+1.0	+16.8	+17.8	+15.8	-2.0
208	+16.0	-9.2	+6.8	+8.5	+1.7
218	+27.0	-34.3	-7.3	-5.6	+1.7
228	+32.9	-53.2	-20.3	-18.0	+2.3
238	+34.7	-58.7	-24.0	-22.2	+1.8
248	+32.9	-49.8	-16.9	-19.1	-2.2
258	+27.0	-31.3	-4.3	-10.2	-5.9
268	+16.0	-9.7	+6.3	+3.5	-2.8
278	+1.0	+8.4	+9.4	+15.2	+5.8
288	-14.1	+18.7	+4.5	+13.0	+8.5
298	-23.8	+17.3	-6.5	-4.6	+1.9
308	-23.3	+8.7	-14.6	-21.9	-7.3
318	-12.3	-2.3	-14.6	-21.4	-6.8
328	+4.6	-10.7	-6.1	-4.2	+1.9
338	+19.4	-13.5	+5.9	+13.2	+7.3
348	+25.0	-8.5	+16.5	+19.3	+2.8
358	+19.4	+1.2	+20.6	+17.7	-2.9
8	+5.6	+11.7	+17.3	+14.7	-2.6
18	-8.2	+18.5	+10.3	+8.8	-1.5
28	-20.9	+16.5	-4.4	-4.1	+0.3
38	-25.9	+4.5	-21.4	-21.5	-0.1
48	-26.6	-12.8	-39.4	-39.2	+0.2

It has long been known that the eccentricity of the magnetic dipole coincides with the equatorial major axis of the triaxial Earth and that the minor axis of the equator points towards the point of convergence of the magnetic secular variation². I have approximated the equatorial section of the geoid by zonal spherical harmonics in a way that makes use of the axially-symmetrical features of zonal spherical harmonics. It emerges that the equatorial section of the geoid can be approximated by the sum of two rigorously symmetrical geometrical forms³ (Fig. 1).

By varying the direction of the axes of the two symmetrical geometrical figures, it is possible to choose a best fit solution; the directions corresponding to this best fit are 58° and 156.5° E.

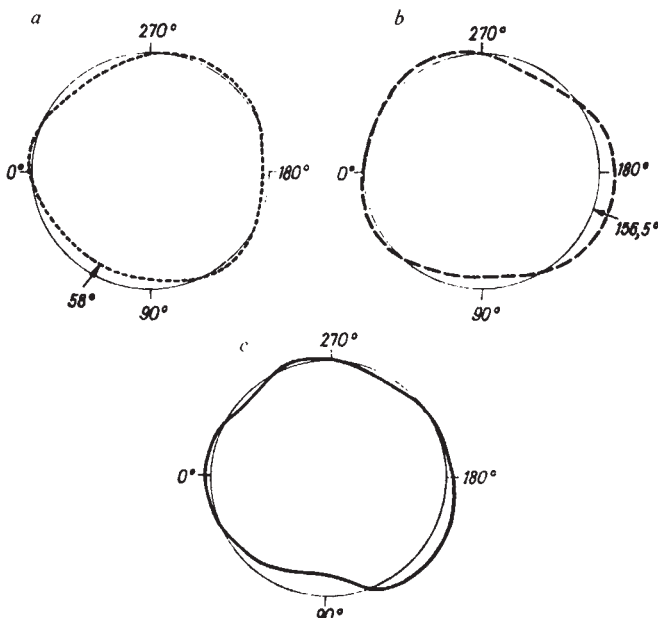


Fig. 1 Approximation of the equatorial section of the geoid by two symmetrical forms from the directions 58° and 156.5° E. *a* and *b*, Symmetrical forms; *c*, their sum.

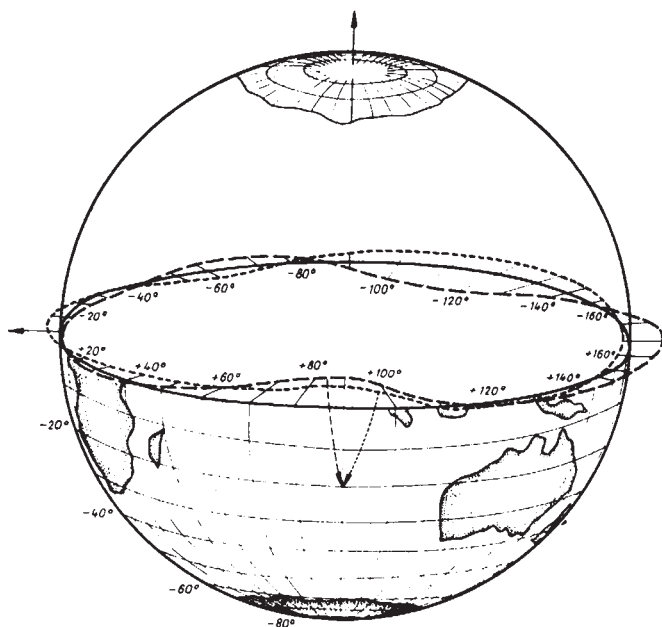


Fig. 2 Computation of the geoid figure from two rotation-symmetrical anomaly systems.

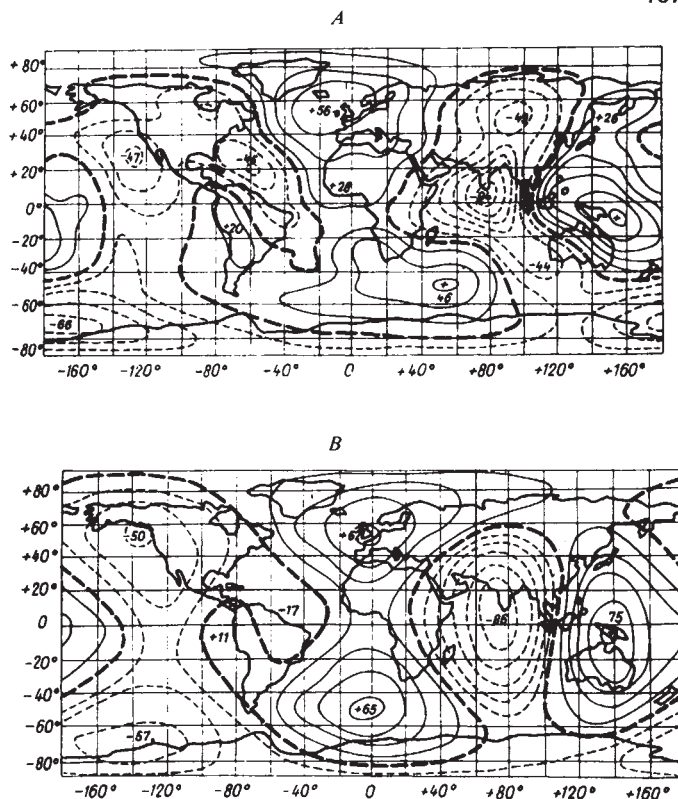


Fig. 3 *A*, The "Smithsonian 1966" geoid; *B*, geoid figure computed from the two rotation-symmetrical anomaly systems. Spacing of isolines, 15 m.

The computations were made in 1969–70 and were based on the equatorial profile of the Smithsonian Standard Earth, 1966. The basic anomalies of the more recent geoids do not differ significantly. The form of these approximating functions is as follows:

$$\begin{aligned}\Sigma_1 &= -0.3 - 3.70 P_{20} - 46.11 P_{30} + 8.16 P_{40} + 15.56 P_{50} \\ \Sigma_2 &= -11.8 + 61.74 P_{20} + 43.50 P_{30} - 25.13 P_{40} - 5.10 P_{50},\end{aligned}$$

where P_{40} are the zonal spherical functions related to the point 58° E of the equator as polar point, or for the point 156.5° E. The positions of the symmetry points and the form of the functions refer to the geoid under consideration only, but a more general validity may be attributed to them because of the similarity of geoid figures obtained in different ways.

Substituting into the zonal harmonics the angle of distance of the single points from the corresponding polar point gives the single symmetrical anomaly components of the equatorial section, the sum of which closely approximates the actual section (Table 1).

Assuming the rotational symmetry of the anomalies thus obtained in the equatorial plane and computing the spherical distance measured from the approximating directions for the grid of points having integer coordinates, one easily obtains a map-like distribution of the anomaly components sum over the globe's surface (Fig. 2). By eliminating the polar flattening in the course of summation and by taking into account the well known pear-shape of the Earth, a theoretical geoid figure is obtained (Fig. 3).

The geoid figure thus computed is similar to and even identical with the measured figure as regards both the position and the size of anomalies.

It is important that I have used for the construction of the computed geoid merely the equatorial data system of measurements. The identity of these two figures cannot therefore be regarded simply as a result of approximation, but it can be considered as a proof of the fact that the

complex geoid figure is merely the sum of two rotation-symmetrical anomaly systems and no other agents play an important role in the formation of the geoid pattern.

Certain further conclusions may also be drawn from the coefficients of the approximating functions. The zonal harmonic series connected with the direction towards Australia converges uniformly and the coefficients of the successive terms of even and odd degree are regularly decreasing. On the other hand, the even terms of the function in connexion with India are small compared with those of odd degree, that is, this form shows no ellipticity.

The coefficients of the mathematical formulae and the figure that can be computed with them support the hypothesis that—according to the eccentricity of the magnetic field—a deep-lying positive inhomogeneity of material character exists in the direction of Australia; nearly perpendicular to this, near the symmetry-point of the secular magnetic variation, a similarly essential geoid deformation exists, associated, however, with energy effects.

Besides the high degree of similarity, the theoretical and the measured geoid patterns also show certain characteristic differences. The axes of the positive and negative anomaly systems of the northern, resp. southern hemispheres—measured on the map—are not perpendicular to the line of the Equator. Consequently, when determining the position of the responsible density inhomogeneity, one has to step out of the Equator. By that means, a still better approximation than the present would be obtained.

From the foregoing it is clear that the geoid is the result of two effects originating at great depth and in all probability is not linked with the distribution of oceans and continents on the surface of the globe. The starting point of this study is the coincidence of the direction of eccentricity of the magnetic dipole with the great positive geoid anomaly over Australia. If the two phenomena are causally related, one must suppose the existence of a secular variation of the gravity field as well as of the geoid.

G. BARTA

Department of Geophysics,
Eötvös University,
Budapest

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Yellowstone Convection Plume and Break-up of the Western United States

MUCH of the late Cainozoic history of the western United States is characterized by tensional rifting. The Basin and Range Province is a zone of rifting 300 to 600 km wide (Fig. 1). The Rio Grande depression and the Snake River downwarp are areas of rifting which are similar in time and style to the Basin and Range faulting. The rifting in the Rio Grande depression has usually been related to the same causative mechanism as in the Basin and Range. The Basin and Range type faulting has variously been explained as the result of a westward moving convection cell¹; as part of a wide, soft boundary reflecting the transform motion of the American and Pacific plates²; or as the result of a large mantle diapir which came up under the crust following the complete subduction of the Farallon plate in that region³. Although most of these explanations adequately account for the Basin and Range faulting, they fall short in explaining the rifting in the Rio Grande depression. None of the three hypotheses adequately explains why extensive rifting occurs over a area 600 km wide in the Basin and Range abruptly stops for a length of 500 km in the Colorado Plateau area and

then resumes again in a narrow zone in the Rio Grande region. The Snake River rifting transects the regional trend of the Basin and Range rifting and does not fit any of the proposed tectonic models for the Basin and Range.

We propose that the mechanism of rifting in the Rio Grande depression and Snake River downwarp is different from the mechanism of rifting in the Basin and Range region. The rifting in the Rio Grande region of the Southern Rocky Mountains and in the Snake River Plain is the result of the break-up of the western United States by the Yellowstone convection plume, whereas the Basin and Range faulting may be a result of one of the three previously mentioned hypotheses.

The Snake River downwarp (Fig. 1) is an arcuate graben more than 500 km long that has formed since early Pliocene⁴. The depression is filled with continental detrital sediments and tholeiitic basalt flows⁴. Thickness of the fill is estimated to range from 100 to 1,500 m in the eastern part of the depression⁵ and may exceed 3,000 m in the western part⁶.

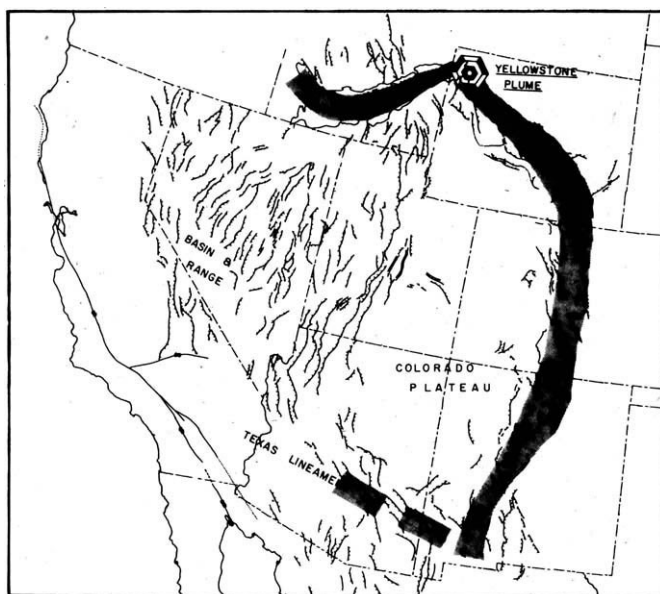


Fig. 1 Index map of western United States showing normal and reverse faulting, location of the Yellowstone convection plume, and the approximate boundaries (shaded areas) of newly forming plate. (Low-angle thrust faults are not included on this map.)

The Rio Grande depression is a late Cainozoic feature which extends from southern New Mexico 800 km into central Colorado (Fig. 1). It is a complexly faulted graben which may contain as much as 10,000 m of fill⁷. Basalts with alkalic affinities and those with tholeiitic affinities are spatially related to the depression in the same manner as the tholeiitic basalts and alkali olivine basalts are spatially related to the East African rift valley⁸.

The volcanic activity in the Yellowstone region has been attributed to a mantle convection plume located under that area^{9,10}. Interpretations of absolute motions of lithosphere plates indicate that North America has been moving very slowly over the Yellowstone plume for the past 40 m.y. (refs. 10 and 11). A lithosphere plate which is stationary or moving slowly over a mantle convection plume presumably will break up into two or more smaller plates. A convection plume in the vicinity of the Afar triangle seems to be causing the rifting in the Red Sea, Gulf of Aden, and East African rift valley. We propose that the Yellowstone plume is causing the break-up of the American plate in a somewhat analogous manner. Most of the western United States is part of a new plate which is trying to break free from the rest of the American plate.

Boundaries of the newly forming plate are the Snake River downwarp, Middle and Southern Rocky Mountains, Rio

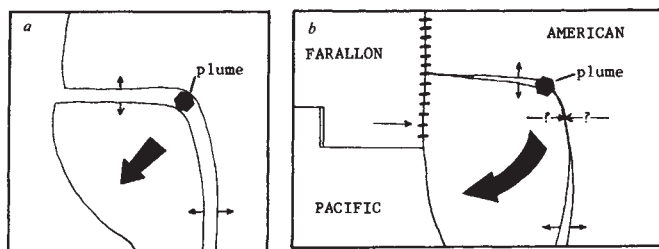


Fig. 2 *a*, Example of ideal case where rifting and break-up of lithosphere results from slow movement over a convection plume; *b*, rifting that might result from break-up of western United States by Yellowstone plume. Trench boundary along northern part of west coast during the late Miocene would act as a barrier to movement, while the southern part would be free to move. The resulting motion would be a somewhat clockwise rotation of the new plate.

Grande depression, and possibly the Texas Lineament (Fig. 1). Under ideal circumstances, a plume causing the break up of a plate would propagate cracks away from the plume with subsequent rifting as illustrated in Fig. 2*a*. Although the Snake River downwarp extends outward from the plume, the Rio Grande depression begins some 800 km from the plume. Obviously this distribution of rifting does not resemble the ideal case. But the late Cainozoic plate tectonic history of the west coast of the United States provides a possible explanation for the distribution of rifting and uplift around the margins of the new plate.

Although the American plate has been moving very slowly over the Yellowstone plume for the past 40 m.y., the plume may not have been effective in breaking up the plate until more recently because of the interaction of the Farallon plate with the American plate during the late Cainozoic. Before 29 m.y. ago a trench boundary between the American plate and the Farallon plate existed off the entire coast of the western United States. Underthrusting by the Farallon plate probably acted as a barrier to the westward movement of the newly forming plate. The trench boundary changed to a transform fault boundary when the Pacific plate came in contact with the American plate.

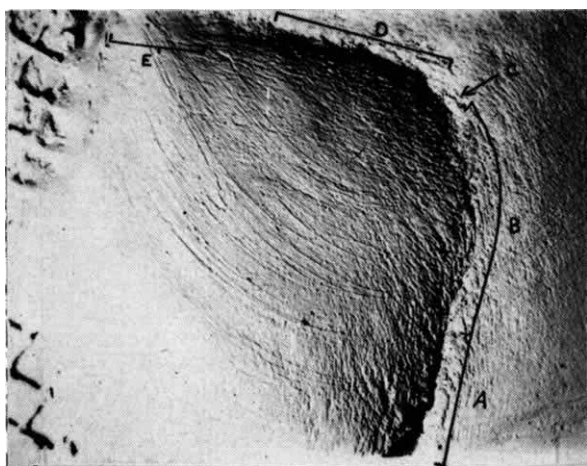


Fig. 3 Clay cake simulation of movement of new plate. Rigid wire mesh was placed partially under clay cake with apex located at C. The rigid wire mesh was given a combination of tension and clockwise rotation away from C. A large rift (0.5 cm) developed in region A similar to the Rio Grande depression. Minor breaking occurred in area B which is analogous to middle and southern Rocky Mountains. In nature, this minor breaking would cause isostatic adjustment in the mantle and uplift of the Rockies in the late Cainozoic. The Yellowstone plume is represented by C. Area D is another significant rift (0.4 cm) which corresponds to the Snake River downwarp. Area E is an area of little or no faulting.

Therefore, once the trench was shut off, the new plate was able to break free. But the entire trench was not shut off at the same time. It first disappeared off northern Baja California¹². Elimination of the trench then progressed from Baja California northward to its present location off Cape Medici¹². This set the southern part of the new plate free to rift while still acting as a barrier to the northern part. The resulting motion would be a clockwise rotation away from the Yellowstone plume as depicted in Fig. 2*b*.

To test this idea, we performed clay cake experiments in which a rigid plate under the clay cake, with its apex representing the Yellowstone plume, was given this type of rotational movement. Fig. 3 shows that the resulting distribution of the rifting is nearly identical to that in the western United States. A large rift developed near the apex (Yellowstone plume), similar to the Snake River downwarp. Another large rift developed at some distance from the apex, similar to the Rio Grande rift which developed at some distance from the Yellowstone plume. Late Cainozoic uplift in the Middle and Southern Rocky Mountains can be attributed either to compression resulting from the rotation or to uplift prior to major rifting.

VINCENT MATTHEWS III
C. E. ANDERSON

Department of Earth Sciences,
University of Northern Colorado,
Greeley, Colorado 80631

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Dislocation Vibration as a Possible Cure for High Temperature Void Formation in Metals under Fast Neutron Irradiation

EXTENSIVE void formation occurs in metals subjected to fast neutron irradiation in the temperature range of $0.3 T_m$ to $0.5 T_m$ where T_m is the melting temperature of the metal¹⁻⁴. This phenomenon is a serious problem in reactor technology. In conditions of fast neutron irradiation large numbers of lattice vacancies and interstitial atoms are produced in equal amounts. Dislocation lines and voids (pre-existing ones or newly nucleated ones) act as sinks to these point defects. If a void is just as efficient a sink for an interstitial atom as for a lattice vacancy and if a dislocation line also is just as efficient a sink for each of these types of defect there can be no tendency for a void to grow²⁻⁴. Equal numbers of vacancies and interstitials will be destroyed in a void as well as at dislocation lines. But dislocation lines are probably a more efficient sink for interstitials than for vacancies. Thus more interstitials are destroyed at dislocation lines than are vacancies. The excess vacancies are destroyed at voids, causing them to grow. This very plausible explanation has been presented in the literature

to account for growth of voids (see refs. 2-4 and the references cited there).

If a dislocation can be made to be as efficient (or more efficient) a sink for vacancies as for interstitials, void growth will be prevented. Here we point out how a dislocation can be made a better sink for vacancies.

The theory that Ham⁵ developed for impurity segregation to a dislocation line has been applied² to show that in general an edge dislocation is a better sink for interstitials than for vacancies. If an edge dislocation line has no stress field associated with it diffusion of point defects to it is equivalent to diffusion in a cylinder of inner radius b , where b is the Burgers vector of the dislocation, and outer radius R , where R is half the mean spacing between dislocations. The defect concentration at the inner radius is the equilibrium concentration appropriate to the temperature of the metal. The concentration at the outer radius is greater than the equilibrium concentration because of the defects produced by the neutron irradiation. An edge dislocation does, however, have a stress field and vacancies and interstitials will interact with this field. Ham showed how this interaction affects the diffusion around a dislocation. The effect of the interaction is to increase the "effective" inner radius of the cylinder from b to a value that increases with the strength of the interaction. The larger the effective value of the inner radius, the better sink is the dislocation line. Because interstitials interact more strongly with the stress field of an edge dislocation than do lattice vacancies, the dislocation is a better sink for interstitials than for vacancies. The calculations of Harkness and Li² seem to indicate that the effective inner radius for interstitials is increased by about $2b$. (Bullough and Perrin³ concluded that to make a fit to experimental data a dislocation line is a 1 to 2% better sink for interstitials than for vacancies.)

If a dislocation which is acting as a sink for point defects is set into oscillatory motion of frequency ν and amplitude λ where $\lambda > b$, then in a time $t = 1/\nu$ the characteristic diffusion distance d for the point defects is approximately given by $d \sim \sqrt{(D/\nu)}$, where D is the diffusion coefficient of either the vacancies or of the interstitials. If $d \gg \lambda$ the diffusion takes place at such a fast rate that for all practical purposes the dislocation can be considered to be a stationary sink for the point defects. But if $d \sim \lambda$ or if $d < \lambda$ the dislocation moves back and forth quickly enough so that it can be considered to be a sink for point defects with a dimension on the slip plane (or an "effective" inner radius) of λ rather than b . Clearly in this situation the dislocation is a more efficient sink than when it is not vibrating.

Interstitial atoms in metals diffuse with such high velocities in the temperature range in which void formation is extensive that it is very difficult to make a dislocation a better sink for interstitials by vibrating the dislocation. For example, stainless steel² forms voids in the temperature range 300° to 600° C. The diffusion coefficient D for interstitials in this temperature region calculated using the activation energies for diffusion estimated by Harkness and Li² or by Bullough and Perrin³ is of the order of 1 to 10 mm² s⁻¹. For frequencies of 1 Hz to 1 kHz the diffusion distance d is in the range 0.03 to 3 mm. It would be impractical to vibrate dislocations with an amplitude comparable to these values of d .

Vacancies in metals diffuse much more slowly than do interstitial atoms. For stainless steel in the temperature range of 300 to 600° C the estimated value of D (refs. 2 and 3) is of the order of 6×10^{-7} to 3×10^{-11} mm² s⁻¹. At frequencies of 1 Hz to 1 kHz the diffusion distance d is between 2×10^{-7} mm and 8×10^{-4} mm. Certainly it is practical using moderate oscillating stresses to force dislocations to vibrate with amplitudes in the lower part of this range, say, 2×10^{-7} mm to 2×10^{-5} mm. Thus it seems that by forcing them to vibrate it is possible to make dislocations better sinks for vacancies. It may be possible, therefore, to eliminate void formation, at least in the lower part of the temperature range in which voids form through forcing dislocations to vibrate. The technique of

vibrating the dislocations under cycle stresses can be used to obtain new experimental information on the relative efficiency of dislocations as sinks for interstitials and for vacancies.

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W. V. GREEN

Los Alamos Scientific Laboratory,
Los Alamos, New Mexico 87544

J. WEERTMAN

Los Alamos Scientific Laboratory, and
Materials Science Department,
Northwestern University,
Evanston, Illinois 60201

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Field Observations of Edge Waves

EDGE waves are solutions for wave motion trapped against a shoaling beach. Their amplitude varies sinusoidally along the shore and diminishes rapidly seawards from the shoreline. Eckart¹ has shown that there is a family of edge wave solutions of the shallow water equations. Each solution is characterized by a mode number which gives the number of zero crossings in the seaward decay of amplitude; each mode has a dispersion relation linking the longshore wavenumber with the edge wave frequency.

Edge waves have been observed in the laboratory; Bowen and Inman² showed that waves of a single frequency ω approaching the shore can excite edge waves close to the same frequency or at the subharmonic frequency $\omega/2$. The existence of edge waves on natural shorelines has been inferred from the periodic spacing of rip currents² and the existence of beach cusps and crescentic bars³ but no previous direct measurements of the water motion associated with edge waves on natural beaches have been reported. Here we present preliminary results, from field measurements of water currents close to the shore, which strongly suggest the existence of a subharmonic, zero order edge wave.

The measurements were made during August 1972 at Slapton Beach, South Devon. This is a shingle ridge running in a gentle curve for more than 5 km. Surveys showed that the beach profile in the inter-tidal zone could be approximated by the expression

$$h = h_0(1 - e^{-ax}) \quad (1)$$

where h is the water depth at high tide, x the offshore coordinate and for Slapton Beach $h_0 = 7.05$ m and $a = 3.14 \times 10^{-2}$ m⁻¹.

The onshore and longshore horizontal components of the water current were measured by an electromagnetic flowmeter⁴ held 0.3 m above the seafloor on an aluminium base. The flowmeter was placed in a fixed position in the intertidal zone so that with the incoming and receding tide its distance from the shoreline varied from 0 m to 11 m and back to 0 m within a 4 h period spanning the time of high water. During this period current meter readings were logged digitally every 0.5 s for separate runs of duration of 15 min.

Spectral analyses of four pairs of fifteen minute time series obtained on August 10, 1972, have been made using the fast Fourier transform technique and a smoothing filter⁵; a typical spectrum of current amplitude is shown in Fig. 1. The fast rise in the spectrum to a broad peak followed by a steady

decay with increasing frequency is typical of a wind wave spectrum, and the broad peak occurs at around 0.2 Hz, corresponding to the observed breaker frequency in the surf zone. An unusual feature of the spectrum, however, is the rather sharp peak at about 0.1 Hz, about one half of the predominant wind wave frequency. This energy peak occurs in each of the spectra and for both onshore and longshore components of the flow.

The variation with offshore distance of this energy at 0.1 Hz suggests that it is due to the presence of an edge wave. In Fig. 2 the triangles represent the measured r.m.s. amplitudes at 0.10 ± 0.02 Hz plotted as a function of the offshore position of the current meter, for onshore (Fig. 2a) and longshore (Fig. 2b) components of the flow. Because the breakpoint occurred at about 6 m from the shoreline it is clear that the amplitude continues to increase well into the surf zone. In contrast, other peaks, including the wind wave peak at 0.2 Hz, showed a slight rise towards the breakpoint and then became indistinguishable inside the surf zone. Any edge wave at the incident wave frequency itself, if present at all, was of very small amplitude.

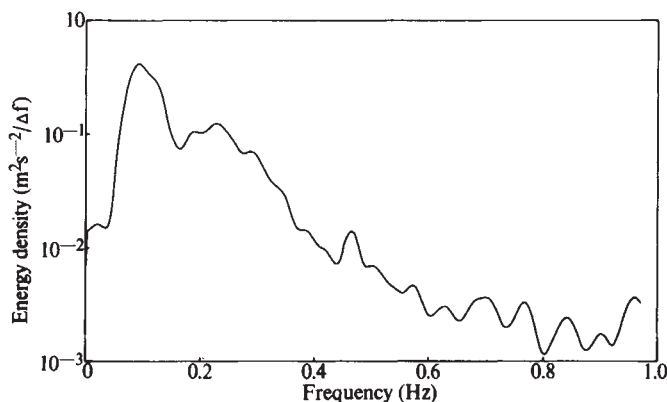


Fig. 1 A typical onshore current spectrum, showing the wind wave peak at 0.2 Hz and the additional peak at 0.1 Hz. The offshore distance was 9.0 m. $N=1,536$; $\Delta t=0.5$ s; $\Delta f=0.025$ Hz.

It is not possible to explain the observed amplitudes at 0.1 Hz in terms of a standing gravity wave formed by reflexion at the shoreline, because that would lead to quadrature of the longshore and onshore current components, whereas the observed components are found to be in phase with each other.

The ratio of onshore to longshore current amplitudes is approximately constant, independent of offshore position, at 4.6 ± 1.0 . This is consistent only with the $n=0$ edge wave mode and would be inconsistent with any higher order mode. Because the value of the ratio is not unity, as would be expected for a progressive edge wave, the currents must be associated with a trapped standing edge wave. This is confirmed by the observed phase relationship between the horizontal current components because a progressive edge wave implies phase quadrature whereas a standing edge wave gives the observed in-phase relationship. For a standing edge wave, the observed amplitude ratio shows that the current measurements must have been made about 1.3 m along the shore from a longshore current node.

Using the dispersion relations derived by Ball⁶ for a beach with a profile given by equation 1, we have calculated the predicted wavelengths of 0.1 Hz edge waves for Slapton Beach, and find for the zero mode a wavelength of 32 m. Ball's theory shows that the zero mode edge wave decays exponentially with distance from the shoreline, with a decay constant dependent on the edge wave wavelength L and the slope parameter a .

Accordingly we have plotted (Fig. 2) the exponential decay corresponding to an edge wave of wavelength 32 m. The

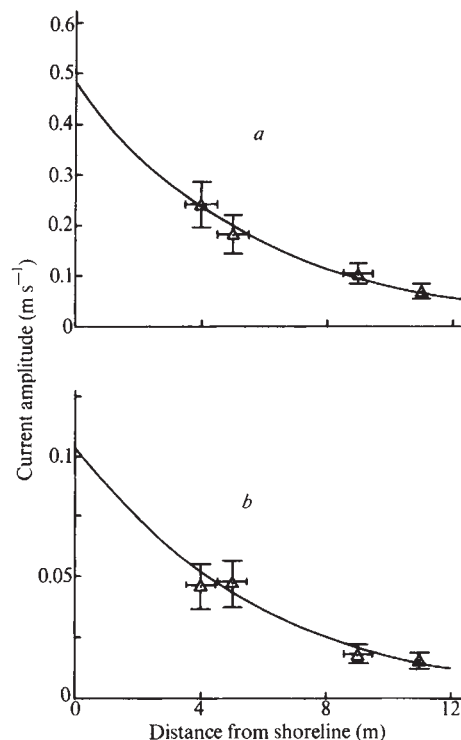


Fig. 2 Graphs of onshore (a) and longshore (b) current amplitude at 0.1 Hz plotted against distance from shoreline. The solid line shows the expected decay for an edge wave of the predicted wavelength of 32.0 m. The measured values are shown as triangles with amplitude error bars corresponding to the 80% confidence limits in the spectral analysis; horizontal errors are a consequence of averaging amplitudes during an incoming tide.

measured values fit the expected edge wave curve to within the statistical uncertainty. The least squares best fit of the data to an exponential curve gives $L=34 \pm 5$ m for the onshore current and $L=34 \pm 6$ m for the longshore current.

The longshore variation in horizontal excursion of water up the beach expected from the observed edge wave would have been too small (horizontal amplitude ≈ 0.5 m) to be observed above the general irregularity caused by the incoming waves. Any tendency of the edge wave to form beach cusps may have been overridden by the oblique angle of approach of the waves which was about 10° from normal at the breaker line. In fact there were no obvious variations in longshore topography which could have induced the observed nearshore motion⁷.

These results from a fairly steep beach with small incident waves may have important implications for the mechanism of edge wave generation. Bowen and Inman² remark on an apparent correlation in their laboratory experiments between the amplitude of edge waves and the magnitude of the standing wave caused by reflexion of the incident wave at the beach. Trapping of the edge wave may seem rather unexpected because the edge wavelength of 32 m is small in comparison to the length of the beach, which extended about 2.5 km on either side of the point where measurements were made. But standing edge waves are also suggested by crescentic bars which are known to occur on long straight beaches as well as in confined bays³. The mechanism responsible for generating edge waves may favour the formation of standing rather than progressive edge waves.

D. A. HUNTLEY
A. J. BOWEN

*Institute of Coastal Oceanography and Tides,
Bidston Observatory,
Birkenhead,
Cheshire*

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BIOLOGICAL SCIENCES

Oncogenic Transformation of Hamster Embryo Cells *in vitro* by Adenovirus Type 5

JUDGED on the basis of virus inoculation tests in newborn hamsters¹, human adenovirus type 5 is considered to be non-oncogenic. The virus does transform rat embryo cells with low efficiency *in vitro*^{2,3}, although these cells do not form tumours in rats (my unpublished results). Infection of hamster cells *in vitro* with type 5 adenovirus gives rise to a productive infection (ref. 4 and my unpublished results) and most of the cells are killed. Because of this extensive cell killing transformation of hamster cells by adenovirus type 5—if it does occur—is unlikely to have been detected. To determine if adenovirus type 5 can transform permissive cells, hamster embryo fibroblasts (HEF) were infected with temperature sensitive (*ts*) mutants⁵ at the restrictive temperature which prevents cell killing caused by virus replication. The mutants used transform non-permissive rat embryo cells at the restrictive temperature (my unpublished results) with frequencies similar to wild type virus, thus the viral function(s) involved in transformation of those cells are not affected by these particular *ts* mutations.

In the work described here, secondary cultures of HEF were infected with one of the *ts* mutants *ts1*, *ts4* or *ts14* at an input multiplicity of 10 plaque-forming units (PFU) per cell. For comparison some cultures were also infected with a similar concentration of wild type virus. For transformation the infected cells (and control non-infected cells) were incubated at 38.5° C for 2 days, then subcultured by seeding at a density of either 4×10^5 or 10^6 cells per 50 mm dish. These subcultures were then cultivated at 38° C for up to 6 weeks. Eagle's medium lacking calcium² and supplemented with 5% calf serum was used for maintenance, and the culture medium was changed every 3 to 4 days.

For measurement of virus replication at 38.5° C and at 31° C some cultures were collected at 40 h and at 120 h after infection respectively. Table 1 shows the virus yields in HEF cells at both temperatures. Whereas wild type virus grows equally well at both 38.5° C and 31° C, the mutants grow almost like wild type virus at 31° C but show little or no growth at 38.5° C as was previously found for the mutants in HeLa cells⁵. Although not shown here, there was less efficient growth of adenovirus type 5 in HEF cells than in HeLa cells; nevertheless the yields represent almost a four log increase over the amount of infectious cell-associated virus detected immediately after adsorption.

In the cultures infected by the *ts* mutants and maintained at 38° C, transformed foci first appeared approximately 4 weeks after infection. After a further week the foci could be clearly distinguished from the non-transformed cell background, and at this time foci were counted. The morphology of these transformed HEF cells (Fig. 1) was similar to that of rat embryo cells transformed by adenovirus type 5 (ref. 3). The results of one complete experiment are shown in Table 2. The transformation frequencies observed on infection with the *ts* mutants are slightly lower than those obtained on rat cells with either wild type virus or with these *ts* mutants (my unpublished results).

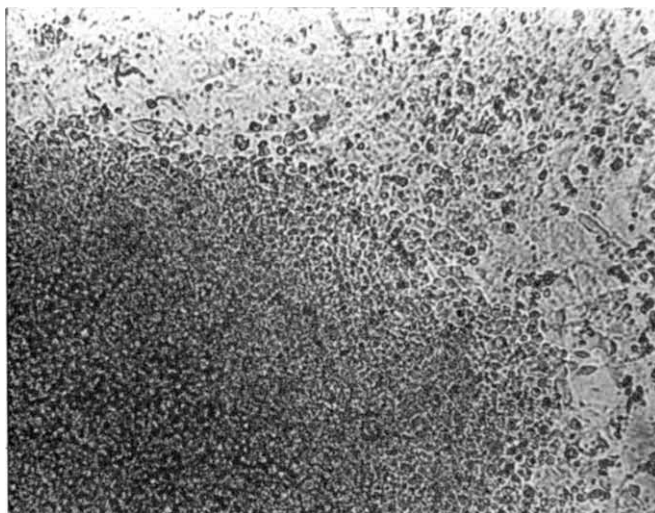


Fig. 1 Focus of HEF cells transformed by adenovirus type 5. Cells infected 30 days previously. Unstained. $\times 60$.

That the same number of foci are produced on dishes seeded with 4×10^5 cells and dishes seeded with 10^6 cells suggests that focus formation may be partly inhibited by non-transformed cells, which rapidly grow to confluence when seeded at higher density.

In this experiment the plating efficiency of the cells infected by wild type virus was reduced to approximately 13% of the plating efficiency of the non-infected controls, and the size of the colonies formed by the survivors was reduced. The plating efficiency of the cells infected by the mutants was also reduced, but to a much smaller extent. Although colonies grew on the dishes seeded with low numbers of wild type infected cells, no cells survived to form colonies on dishes seeded at the higher densities of the transformation assay. The reason for this effect is not established, but it may be due to secondary infection of non-infected cells by contact with primarily infected cells at the higher cell densities.

A number of single foci were picked from cultures infected by each mutant and six lines were established from these. Cells of all six lines retained the transformed morphology throughout many passages *in vitro*. Cells of the lines did not produce virus spontaneously at 38° C, nor were they induced to do so when cultivated at 31° C, the permissive temperature for the *ts* mutants used to transform the cells. The transformed cells could be superinfected by wild type virus (Table 3) at either

Table 1 Yields of Adenovirus Type 5 and *ts* Mutants in HEF Cells.

Virus	38.5° C	31° C
Wild type	$1.2 \times 10^{8*}$	9.0×10^7
<i>ts1</i>	2.0×10^3	4.0×10^7
<i>ts4</i>	1.6×10^4	1.2×10^8
<i>ts14</i>	3.2×10^3	1.0×10^7

Monolayers of HEF cells on 50 mm plastic dishes were infected at an input multiplicity of 10 PFU per cell. Infected cells were collected after 40 h at 38.5° C or after 120 h at 31° C.

* PFU per dish.

Table 2 Transformation at 38° C of HEF Cells by *ts* Mutants of Adenovirus Type 5.

Virus	No. of foci per dish		Plating* efficiency %
	4×10^5 cells	10^6 cells	
Wild type	0, 0, 0	0, 0, 0, 0, 0	0.5†
<i>ts1</i>	2, 2, 3	1, 2, 1, 2, 2	1.7
<i>ts4</i>	2, 2, 1	1, 1, 2	2.1
<i>ts14</i>	2, 2, 1	2, 1, 2, 1, 0	3.2
None	0, 0, 0	0, 0, 0, 0, 0	3.8

* 10^6 cells plated per dish; †, small colonies.

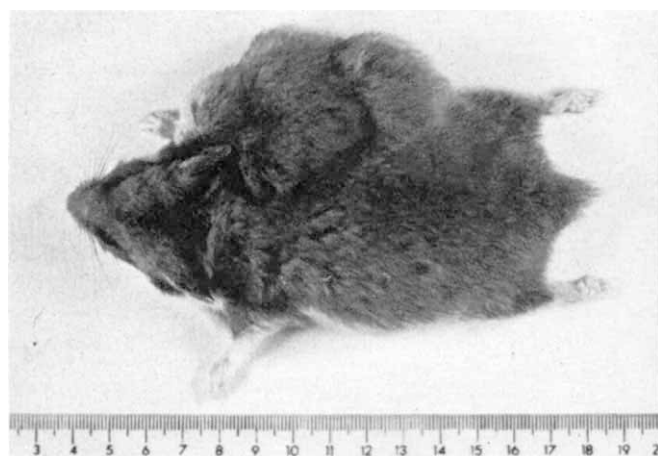


Fig. 2 Subcutaneous tumour in hamster resulting from cells inoculated 60 days previously.

Table 4 Tumour Formation in Baby Hamsters with Embryo Cells Transformed *in vitro* by Adenovirus Type 5

Cells	Passage number <i>in vitro</i>	Age of recipients (days)	Route of inoculation	No. animals with tumours/No. inoculated
Non-transformed				
HEF	15	1	s.c.*	0/11
HT5 14a	5	1	i.p.†	2/8
HT5 14b	5	1	i.p.	2/8
HT5 14a	14	3	s.c.	5/6
Transplant number				
HT5 14a tumour	2	3	s.c.	5/5
HT5 14a tumour	3	3	s.c.	7/8
HT5 14a tumour	4	3	i.p.	4/5
HT5 14b tumour	2	3	s.c.	3/3
HT5 14b tumour	3	14	s.c.	6/7
HT5 14b tumour	4	6	s.c.	5/5

* S.c., Subcutaneous; † i.p., intraperitoneal.
2 × 10⁶ cells inoculated per animal.

temperature and by various *ts* mutants at the permissive temperature of 31° C, although with the mutants used the ensuing yields were lower than the yields attained in non-transformed hamster embryo cells. The capacity for superinfection presents the possibility of detecting virus genes in these cells either by complementation of *ts* mutants at the non-permissive temperature or by production of recombinants at the permissive temperature. So far the results with a few mutants provide no evidence for either interaction in the two transformed lines tested, but the problem is being further investigated using other mutants, and other transformed lines.

Ability to superinfect makes it at least theoretically possible that host range mutants of the type obtained for polyoma⁸ could be obtained. Clearly, these hamster cells transformed by adenovirus type 5 differ from those transformed by adenovirus type 12 (ref. 6), in which superinfection by adenovirus type 2 was not possible. The results suggest the absence of effective repressor or inhibitor in these cells that have been transformed by type 5. We have no evidence that viral genes persist and are active in these cells, but experiments designed to determine if this is the case are in progress.

The cells of two of these lines designated HT5 14a and HT5 14b have been tested for tumorigenicity by inoculation into hamsters. After five passages *in vitro* cells of each of these two lines were inoculated intraperitoneally into 1-day-old hamsters. Approximately 6 weeks later, some of these animals had developed intraperitoneal tumours (Table 4). About 8 weeks after inoculation the tumour-bearing animals were killed, the tumours explanted and grown *in vitro* for two to four passages before reinoculation into 3-day-old baby hamsters. The cells which grew from the tumour explants *in vitro* were morphologically identical to input transformed cells, and they grew rapidly to form tumours when reinoculated into 3-day-old hamsters (Fig. 2). These tumours are transplantable and have been transplanted for up to six consecutive passages. At later passages tumours were formed in 2-week-old recipients, and in adult hamsters. In a few animals metastases to either lungs or liver have been observed. Non-infected, non-transformed

hamster cells passaged *in vitro* fifteen times failed to develop tumours in 1-day-old hamsters, suggesting that the oncogenicity of the adenovirus-transformed cells was not spontaneously acquired. The results of some of the transplantation tests are shown in Table 4.

The histology of the tumours has been examined by Dr J. M. Vettors of the Pathology Department, Glasgow University. They appear to be largely of the small cell sarcoma type or possibly malignant lymphoid neoplasms with necrotic centres typical of tumours induced by the oncogenic adenoviruses.

The results indicate that adenovirus type 5, until now considered to be a non-oncogenic adenovirus, is capable of oncogenic transformation of cells *in vitro*. Attempts are being made to determine if the wild type virus or the *ts* mutants can induce tumour formation after inoculation of newborn hamsters.

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J. F. WILLIAMS

MRC Virology Unit,
University of Glasgow,
Glasgow

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Table 3 Growth of Adenovirus Type 5 in HEF and Transformed HEF (HT) Cells at 38.5° C.

Experiment	Cells	Virus yield	
		0 h†	40 h
1	HEF	8.5 × 10 ⁴	2.3 × 10 ⁸ *
1	HT5 14b	3.8 × 10 ⁴	4.4 × 10 ⁸
2	HT5 1a	4.4 × 10 ³	3.0 × 10 ⁷
2	HT5 4a	3.0 × 10 ³	2.0 × 10 ⁷

Monolayers were infected at an input multiplicity of 10 PFU per cell. *, PFU per dish; †, immediately after absorption.

α-Bungarotoxin used as a Probe for Acetylcholine Receptors of Cultured Neurones

THE snake venom protein α-bungarotoxin binds with specificity and high affinity to nicotinic acetylcholine receptors of striated muscle¹⁻⁶, electric tissues⁷⁻⁹, and mammalian brain¹⁰. For these reasons, this toxin, as well as similar

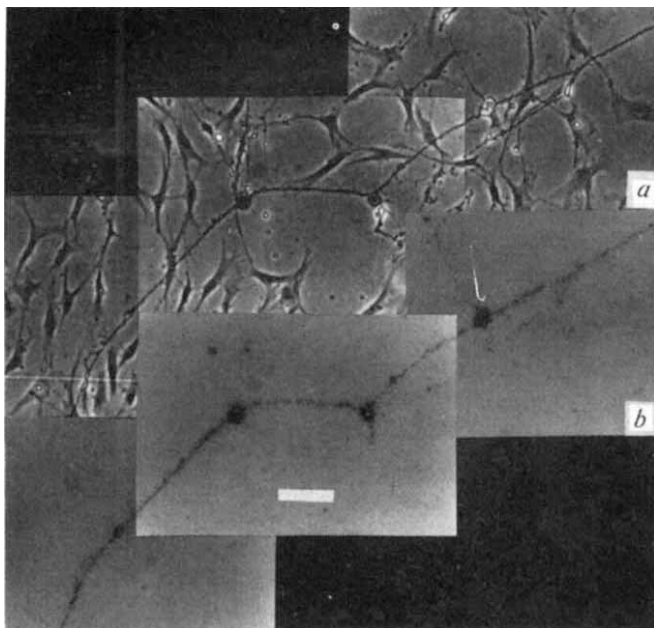


Fig. 1 Autoradiography of cultured cells from chick embryo sympathetic ganglia after incubation with ^{125}I -diiodo- α -bungarotoxin. Chains of paravertebral sympathetic ganglia from 11-day chick embryos (white Leghorn) were incubated in Ca, Mg-free Dulbecco's phosphate-buffered saline¹⁸ containing 0.25% trypsin (Difco, 1 : 250) for 30 min at 37°C. The trypsin was removed and the chains were washed twice with complete culture medium (95% F-14 medium¹⁹, 5% foetal bovine serum, and 10 ng (2 units) of nerve growth factor protein¹⁷ per ml. of medium) and then dissociated by gentle trituration¹⁵. 1.0×10^5 cells were added in 2 ml. of complete media to collagen-coated 35 mm tissue culture dishes (Falcon). Maintenance of the cultures as well as their incubation with the labelled toxin was at 37°C in an atmosphere of 10% CO_2 -90% air saturated with H_2O . The cells shown in the figures were maintained *in vitro* for 5 days. The growth medium was then replaced with 1 ml. of incubation medium (F-14 medium without choline and with 2 mg ml^{-1} of crystalline bovine serum albumin) containing 5×10^{-9} M ^{125}I -diiodo- α -bungarotoxin (2.2×10^5 Ci mol^{-1} toxin). After incubation for 1 h the dishes were washed at room temperature four times with 2 ml. portions of incubation medium and twice more with 2 ml. portions of F-14 (minus choline). Cells were fixed in 0.1 M sodium phosphate buffer (pH 7.4) containing 2.5% glutaraldehyde, and were subjected to autoradiography with Kodak NTB-2 emulsion for 8 days²⁰. The same field is shown in *a* and *b*. Phase contrast optics were used to show cell structure (*a*), and bright field optics to show silver grains of the autoradiograph (*b*). The bar corresponds to 50 μm .

toxins from elapid snakes, has been used for labelling, purifying and assessing the physicochemical properties of cholinergic receptors.

Another possible use of α -bungarotoxin is to probe acetylcholine receptors of intact neurones. The toxin could be used to identify neurones possessing nicotinic receptors as well as to examine properties of the receptor such as concentration, distribution and pharmacology. Probing neuronal acetylcholine receptors in the intact nervous system is hindered, however, because individual neurones tend to be inaccessible to substances of high molecular weight and are difficult to view. One approach to this problem is to dissociate suitable neural tissue and to maintain it as a monolayer in cell culture. Neurones thus obtained and cultured may retain many differentiated properties^{11,12}, are readily accessible and easily viewed, and are in a relatively controlled environment. Neurones obtained from chick embryo sympathetic ganglia seem to have certain advantages as a model culture system. Sympathetic ganglion neurones *in vivo* are known to possess acetylcholine receptors of the nicotinic type (for reviews see refs. 13 and 14). Furthermore, chick sympathetic neurones can be obtained in reasonable numbers (approximately 2×10^5 neurones/chick embryo),

are fairly easy to culture and are a relatively homogeneous population.

Here we report that ^{125}I - α -bungarotoxin binds to acetylcholine receptors of cultured chick embryo sympathetic neurones, and hence can be used to probe the properties of these receptors.

Chains of paravertebral sympathetic ganglia from 11-day chick embryos were dissociated with trypsin¹⁵ and cultured in the presence of nerve growth factor^{16,17} as described in the legend of Fig. 1. Cells with the appearance of neurones were quite distinctive after several days *in vitro*; their somas were round and highly refractile, and long, branched processes extended from them (Fig. 1*a*). Such cells did not survive *in vitro* in the absence of nerve growth factor. These cells also possessed electrically excitable membranes and responded to acetylcholine (A. Chalazonitis and L. A. Greene, in preparation). Hence, such cells have properties characteristic of differentiated sympathetic neurones. Other cell types, which probably include fibroblasts, capsule cells and glia were also present and formed a monolayer beneath the neurones within a week.

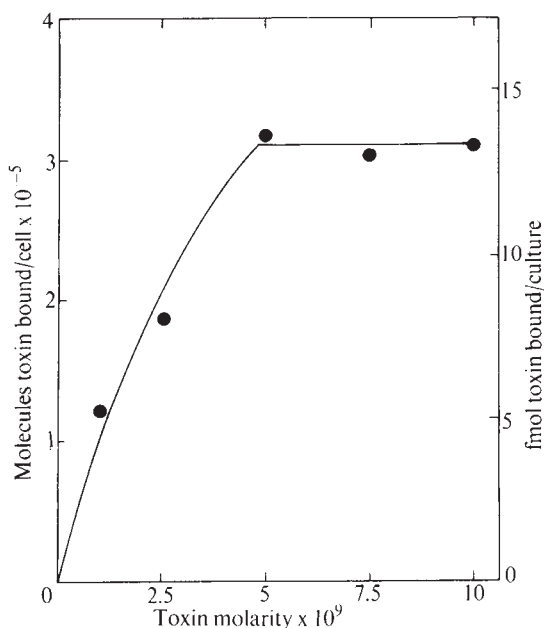


Fig. 2 The relation between α -bungarotoxin concentration and the amount of toxin bound to sympathetic neurones in cell culture. Cells dissociated from chick embryo sympathetic ganglia were seeded at 120,000 cells per dish and maintained *in vitro* for 5 days. The cells were then incubated with various concentrations of ^{125}I -diiodo- α -bungarotoxin (2.8×10^5 Ci mol^{-1} toxin) as described in the legend to Fig. 1. After incubation, cells were washed to remove unbound bungarotoxin, and bound radioactivity was determined as described previously¹⁹. Each value represents the average of triplicate determinations. Reproducibility in this and in other experiments was $\pm 12\%$. The maximum amount of radioactivity bound was 5,600 c.p.m. In the absence of cells, approximately 100 c.p.m. bound to a collagen-coated Petri dish. This value was subtracted from values given in this and other figures. The number of neurones (termed "cells" in the ordinate) was determined as in subsequent experiments, by examining 4% of the surface area of three replicate cultures and counting neurones. The average dish contained $26,000 \pm 3,800$ neurones.

The presence and specificity of a receptor for α -bungarotoxin on sympathetic neurones was examined by autoradiography. After various times *in vitro*, cultures were incubated in the presence of ^{125}I -diiodo- α -bungarotoxin. The preparation and characterization of the labelled toxin have been described previously¹⁹. The cultures were then washed, fixed and subjected to autoradiography²⁰. A representative field of an autoradiograph photographed with phase contrast optics to show cell detail, and then with bright field

optics to show silver grains, is presented in Figs. 1a and b, respectively. In this and other experiments (cells 2 to 22 days in culture), silver grains were localized over sympathetic neurones but not over other cell types. Both neuronal cell bodies and processes were labelled. All cells with neuronal morphology bound toxin but some seemed more heavily labelled than others. Furthermore, the distribution of silver grains over cell bodies and neurites was fairly uniform. No discrete regions with either relatively high or low concentrations of receptors were found, in contrast to the receptor clusters found with cultured chick embryo skeletal muscle^{19,20}.

The amount of α -bungarotoxin bound to cultured neurones was measured by determining the radioactivity retained by the cells after incubation with labelled toxin. Evidence that the radioactivity recovered was bound specifically to sympathetic neurones was obtained from the following observations. As previously pointed out, cultures without nerve growth factor lacked sympathetic neurones but not other cell types. Such cultures did not bind significant levels of labelled toxin. By contrast, cultures with nerve growth factor, and therefore containing neurones, bound the iodinated toxin.

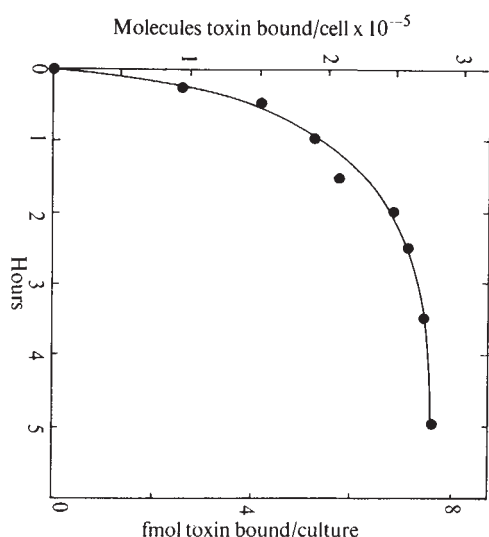


Fig. 3 Time dependence of the binding of labelled α -bungarotoxin to sympathetic neurones in cell culture. Cells dissociated from chick embryo sympathetic ganglia were seeded at 75,000 cells per dish, cultured for 5 days and incubated with 2.5×10^{-9} M 125 I-diiodo- α -bungarotoxin (2.6×10^5 Ci mol⁻¹ toxin) as described in the legend to Fig. 1. Cultures were then washed, and bound radioactivity was determined. Each value represents the average of duplicate determinations. The maximum amount of bound radioactivity was 3,200 c.p.m. The average Petri dish contained $16,500 \pm 3,000$ neurones (termed "cells" in the ordinate).

Binding of the toxin was saturable. As shown in Fig. 2, after incubation for 1 h maximum binding was achieved at a toxin concentration of 5 nM or greater. From the maximum level of toxin bound per culture and from the number of neurones present, the average number of toxin receptors per cell was computed. Assuming that one molecule of toxin binds to one receptor and that the rate of dissociation of toxin from the receptor is relatively low, this number is about 3×10^5 receptors per neurone. The average concentration of receptors on the neuronal membrane was also estimated. Assuming the sympathetic cell bodies to be smooth spheres 10 to 14 μ m in diameter with cylindrical processes 0.6 μ m in diameter and 500 to 1,000 μ m in length (these values are averages measured for the cells in culture), the concentration of receptors on cultured sympathetic

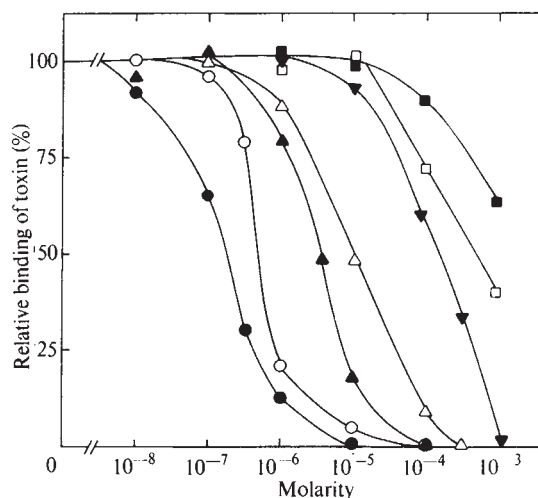


Fig. 4 The effect of ligands of acetylcholine receptors on the binding of 125 I- α -bungarotoxin to sympathetic neurones in cell culture. Cells dissociated from chick embryo sympathetic ganglia were seeded at 70,000 cells per dish and cultured for 4 to 5 days. Cultures were then incubated for 15 min in the presence of the desired final concentration of the appropriate cholinergic ligands. Then 125 I-diiodo- α -bungarotoxin (2.0×10^5 Ci mol⁻¹ toxin) was added in 2 μ l. aliquots (final concentration in the medium = 1.25×10^{-9} M) and the cultures were incubated for an additional 30 min in the presence of both labelled toxin and cholinergic ligand. Cultures were then washed, and bound radioactivity was determined. One hundred % on the ordinate corresponds to 4.7 fmol of toxin (1,500 c.p.m.) bound to cells in the absence of a cholinergic ligand. Each point represents the average of four or five determinations. ●, D-tubocurarine chloride; ○, nicotine dihydrochloride; ▲, 1,1-dimethyl-4-phenylpiperazinium iodide; △, acetylcholine chloride and 1×10^{-6} M eserine sulphate; ▼, decamethonium iodide; □, hexamethonium chloride; ■, atropine sulphate.

neurones is approximately $100\text{--}300 \mu\text{m}^{-2}$. This concentration is similar to that estimated at extrasynaptic areas of striated muscle⁵ and electric tissue²¹ and at areas other than receptor clusters on cultured chick skeletal muscle²⁰, but is two to three orders of magnitude lower than the receptor concentration estimated at the corresponding synapses or clusters^{3-5,20}.

The rate at which the labelled toxin binds to cultured sympathetics is shown in Fig. 3. At a toxin concentration of 2 nM maximal binding was achieved after 3 h of incubation. A semilogarithmic plot of the rate data (assuming that binding is irreversible and that the toxin, in great excess) yielded a rate constant, k_1 , of 1×10^5 M⁻¹ s⁻¹ for formation of the [toxin-receptor] complex. The rate of dissociation of the [toxin-receptor] complex remains to be determined.

Although comparative studies show some variation in receptor specificity among different organisms, selective cholinergic ligands are useful for characterizing and identifying acetylcholine receptors (see refs. 13 and 14 for reviews). Two classical types of acetylcholine receptor have been distinguished—nicotinic and muscarinic. In the mammal, for example, atropine selectively blocks muscarinic receptors, whereas D-tubocurarine selectively blocks nicotinic receptors. Furthermore, at least two varieties of nicotinic receptors have been found. Those of mammalian sympathetic neurones are selectively sensitive to hexamethonium, while those of striated muscle are selectively sensitive to decamethonium²². The pharmacological properties of avian sympathetic ganglion neurones have not been studied to our knowledge.

The specificity of the neuronal receptor for α -bungarotoxin was examined by determining the rate of binding of labelled toxin to cultured sympathetic neurones in the presence of various nicotinic and muscarinic ligands (Fig.

4). Experimental conditions were chosen so that binding of toxin (1.25 nM) was linearly proportional to the time of incubation. The rate of toxin binding was inhibited 50% by 0.25 μ M D-tubocurarine; 0.6 μ M nicotine; 3 μ M 1,1-dimethyl-4-phenylpiperazinium; 10 μ M acetylcholine in the presence of 1 μ M eserine (an acetylcholinesterase inhibitor that had no effect on the binding at the concentration used); 200 μ M decamethonium; and 500 μ M hexamethonium. Atropine, at 1,000 μ M, inhibited binding by only 30%. Also, binding of labelled toxin was completely inhibited by appropriate concentrations of most of the nicotinic ligands used in these studies as well as by a 100-fold excess (125 nM) of unlabelled toxin. Thus, binding of α -bungarotoxin to cultured sympathetic neurones was effectively inhibited by ligands of nicotinic acetylcholine receptors but not by a ligand of muscarinic receptors.

The relatively low potency of hexamethonium in inhibiting binding of toxin to cultured chick sympathetic neurones (50% inhibition at 500 μ M) was somewhat unexpected in light of the potency of this agent in blocking nicotinic receptors on neurones of mammalian sympathetic ganglia²². Species variation between mammalian and avian ganglionic receptors may account for these differences.

The relatively low potency of decamethonium in inhibiting toxin binding (50% inhibition at 200 μ M) provides further evidence for the specificity of acetylcholine receptors on cultured sympathetic neurones. In similar studies with α -bungarotoxin¹⁹, acetylcholine receptors of cultured chick embryo skeletal muscle were at least 500 times more sensitive to decamethonium than were acetylcholine receptors of the cultured neurones reported here. Hence, the selective sensitivity to decamethonium observed with cultured cells resembles that reported for mammalian skeletal muscle and sympathetic ganglia *in vivo*^{14,22}.

These results suggest that the binding sites for α -bungarotoxin on cultured sympathetic ganglia neurones are nicotinic ganglionic acetylcholine receptors. *In vivo* this type of receptor on sympathetic neurones receives excitatory synaptic input from preganglionic neurones in the spinal cord. Alternate interpretations are possible, however. For example, the sites might be the cholinergic receptors suggested to be involved in release of catecholamines²³ or in propagation of nerve impulses²⁴.

In summary, α -bungarotoxin has been used to probe acetylcholine receptors of cultured sympathetic neurones. The distribution, concentration and pharmacological specificity of these receptors were studied. Systems such as the one described here should provide opportunities to identify specific types of neurones with acetylcholine receptors, to distinguish axons from dendrites, to examine the effect of one neurone on acetylcholine receptors of another, to study the regulation and turnover of neuronal acetylcholine receptors, and perhaps to study formation *in vitro* of certain types of synapses.

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LLOYD A. GREENE
ARTHUR J. SYTKOWSKI
ZVI VOGEL
MARSHALL W. NIRENBERG

Laboratory of Biochemical Genetics,
National Heart and Lung Institute,
National Institutes of Health,
Bethesda,
Maryland 20014

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Mutual Antagonism between Botulinum Toxin and β -Bungarotoxin

BOTH botulinum toxin^{1,2} and β -bungarotoxin^{3,4}, isolated from the venom of *Bungarus multicinctus*, have been shown to block neuromuscular (NM) transmission by inhibition of the release mechanisms of the neurotransmitter. The inhibitory effect by either toxin is observed in the rat diaphragm only after a latent period, while the binding of both to the tissue seems to be almost complete during the latent period³⁻⁵. There seem to be two processes for the inhibitory effect, the binding of toxins to the tissue, and the subsequent changes leading to the irreversible inhibition of the release mechanism of neurotransmitter⁴. The time course of the paralysis is markedly accelerated by an increase of stimulus frequency and delayed by procedures or factors which depress the activity of release mechanism, such as deficiency of calcium, increase of magnesium or decreased rate of nerve stimulation⁴⁻⁶. By contrast with botulinum toxin (ref. 2 and our unpublished data), β -bungarotoxin shows an initial facilitatory effect⁴, causing increases of the frequency of the spontaneous miniature end-plate potential and the quantal content of end-plate potential. Questions then arise as to whether or not they bind at a same site and act by a similar mechanism. We therefore studied the interaction between the two toxins in order to investigate the mechanism of the neurotransmitter release inhibition.

We used β -bungarotoxin, isolated by means of CM-'Sephadex' G-50 column chromatography¹, and crystalline botulinum toxin, type A, kindly supplied by Dr E. J. Schantz. The isolated phrenic nerve-diaphragm preparation of the rat was bathed in 50 ml Tyrode solution at 36° C and oxygenated with 95% O₂ + 5% CO₂. The nerve was stimulated with a single supramaximal rectangular pulse every 10 s and the time to cause complete NM blockade was measured. The relations between the time for complete NM block and the concentration of each toxin are illustrated in Fig. 1. The interaction between botulinum toxin and β -bungarotoxin was studied at concentrations of 0.1 and 3 μ g ml⁻¹ respectively. At the respective concentration both toxins blocked the transmission within 150

min when applied alone, but when both toxins were added at the same time, the paralysis was markedly delayed and NM blockade took place only after 250 min, corresponding to a reduction of activity of both toxins by about 90% (Table 1). The same antagonism was also observed when botulinum toxin was applied 30 min after the addition of β -bungarotoxin with or without simultaneous removal of the latter toxin (Table 1).

Table 1 Interactions Between Botulinum Toxin and β -Bungarotoxin

Treatment*		N	Time to paralysis† (min $\pm$ s.e.)	Relative‡ potency (%)
First	Second			
Botulinum toxin	—	12	147 $\pm$ 7	100
β -Bungarotoxin	—	3	126 $\pm$ 4	100
Botulinum + β -bungarotoxin	—	6	253 $\pm$ 27	138.5
β -Bungarotoxin, 30 min	Botulinum	5	217 $\pm$ 14	8.3
β -Bungarotoxin, 30 min then washed	Botulinum	4	237 $\pm$ 9	6.1
Botulinum, 30 min	β -Bungarotoxin	4	174 $\pm$ 13	46

* The rat isolated phrenic nerve-diaphragm preparations were first treated with botulinum toxin (0.1 μ g ml⁻¹) or β -bungarotoxin (3 μ g ml⁻¹), alone or in combination. The second treatment consisted of adding the other toxin 30 min later with or without removal of the first one.

† Time was taken from the addition of the first toxin.

‡ Relative potency of the first added toxin(s) was calculated by comparing with the concentration of uninteracted toxin which would take the same time to cause blockade (see Fig. 1).

§ Calculated against botulinum toxin.

|| Calculated against β -bungarotoxin.

As the binding of β -bungarotoxin to the diaphragm was almost complete within 20 min⁴, this result may indicate an antagonistic effect of botulinum toxin to the bound β -bungarotoxin rather than the formation of an inactive complex between the two toxins. The antagonism is unlikely to be the consequence of a competition or displacement at the binding site in the nerve endings, for either toxin bound to the receptive site would produce paralysis within 150 min by itself. Botulinum toxin evidently retards the inhibitory changes of transmitter release mechanism induced by bound β -bungarotoxin. Further, as the inhibitory effect of botulinum toxin was also decreased in the presence of β -bungarotoxin, it may follow that the binding of or the subsequent inhibitory changes by botulinum toxin is also counteracted by bound β -bungarotoxin. On the other hand, when botulinum toxin was first added and followed

30 min later by β -bungarotoxin, the time to complete blockade was also increased, but to a smaller extent (Table 1).

We suggest that botulinum toxin and β -bungarotoxin act at different sites although their presynaptic effects have many characteristics in common. Because the changes leading to inhibition of the release mechanism after binding with β -bungarotoxin can be retarded by addition of botulinum toxin, however, the binding sites for the two toxins must be closely related. In view of their opposite initial effects, the changes caused in the macromolecule which is involved in the release mechanism after binding of these toxins might be in opposite directions. The mutual antagonism could be thus obtained.

C. C. CHANG
M. C. HUANG
C. Y. LEE

Pharmacological Institute,
College of Medicine,
National Taiwan University,
Taipei,
Taiwan 100

Received December 5, 1972; revised January 18, 1973.

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Anomalous Pigments in the Eyes of the Red-Green Colour Blind

LORD RAYLEIGH noticed that his brother-in-law, Lord Balfour, had abnormal vision and he devised the Rayleigh match to examine it. In rather similar circumstances many years before, Clerk Maxwell used the Maxwell colour triangle to prove that his father-in-law lacked the fundamental red sensation.

Newton was the first to show that spectral red and green, suitably mixed, matched spectral yellow. Rayleigh used a modification of Maxwell's colour box to determine the proportions in which a fixed red and green must be mixed in order to match a fixed yellow. The instrument so used is called an anomaloscope. Rayleigh, whose vision was normal, found that all women agreed with him, but that about 5% of males disagreed, some requiring more red (protanomalous) some more green (deutanomalous).

In his paper¹ he gives the names of his colleagues in the Cavendish Laboratory, Cambridge, who were abnormal, and it is interesting to note among the deutanomalous, Sir J. J. Thomson, Nobel Laureate, who succeeded Rayleigh to the Cavendish chair.

Two kinds of explanations have been suggested for this common and much studied abnormality: (a) Perhaps the visual pigments which determine the eye's spectral sensitivity are abnormal. (b) Perhaps the pigments are normal, but there is abnormality in the way that their nerve messages are processed. Evidence favours (a).

The photoreceptors in the eye, like other photocells, can respond to lights of different wavelengths and are more sensitive to one colour than another. But there is only one dimension of output—the size (not also the quality) of signal—so any two lights can be matched to give identical outputs simply by adjusting their relative intensity.

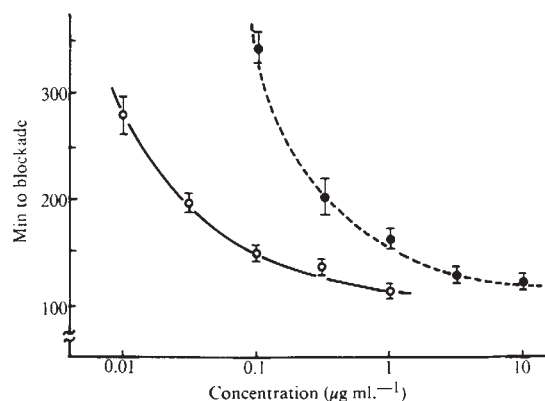


Fig. 1 Time to complete neuromuscular blockade of the rat isolated diaphragm preparation caused by various concentrations of either botulinum toxin (○—○) or β -bungarotoxin (●---●). Vertical bars indicate the standard error of three to twelve experiments.

It follows from this that if the Rayleigh match is so adjusted that the red cones are excited equally by the yellow field as by the (red+green) mixture, they will not be able to distinguish between them. And if at the same time the green cones are equally excited by each field, then they too will be unable to distinguish them and so the two fields will be altogether indistinguishable. (Blue cones are not excited at all by these lights.) This is the condition of the Rayleigh match. If the cone pigments cannot tell apart the two fields, nothing else in the visual system can.

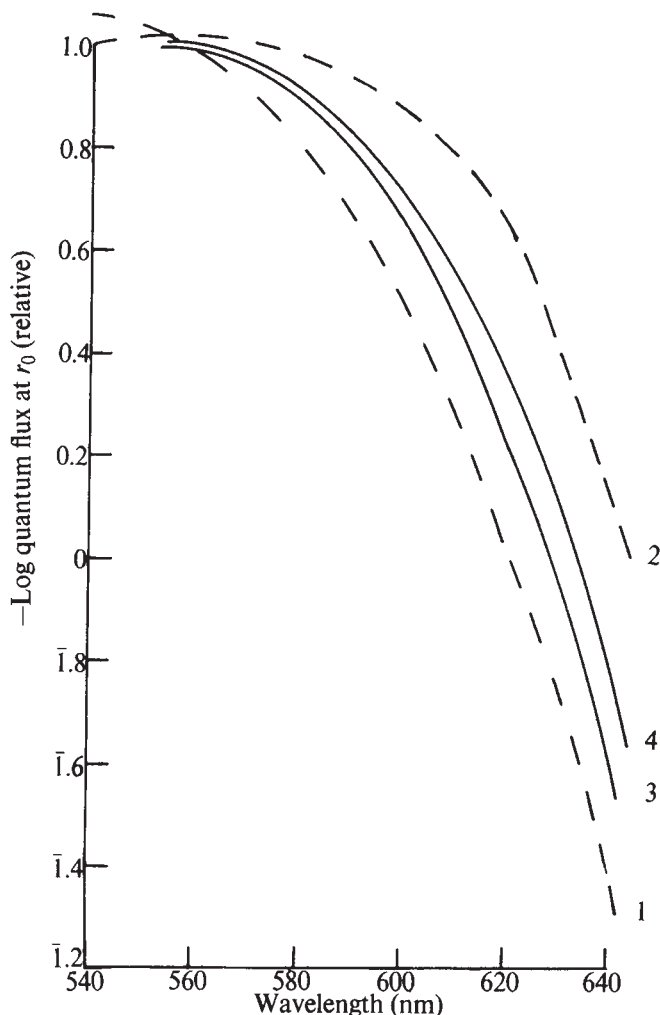


Fig. 1 Log spectral sensitivity curves of four cone pigments. 1, Chlorolabe; 2, Erythrolabe, the "green" and "red" pigments of normal eyes; 3, Protanolabe; 4, Deutanolabe, the pigments of anomalous eyes.

So if Rayleigh's abnormal subjects had normal cone pigments they could not distinguish between two fields that matched for normal pigments whatever the nerve processing. But this is precisely what they can do. Protanomalous insist that the mixture is too green, deuteranomalous that it is too red. They must each possess an abnormal pigment. Over the years, these pigments have proved elusive or their spectral sensitivities would have been discovered long ago. We have measured them at last; here we describe briefly how we succeeded. Full details will be published elsewhere⁶.

For brevity we consider here only the protanomalous type; the deuteranomalous is exactly analogous. One pigment in the eye of the protanomalous is chlorolabe, the green pigment of the normal eye. It is found alone in the protanope, an

extreme case who can match red with green. When he has matched these two lights exactly, naturally he cannot tell when they are exchanged. Thus when protanomalous (or normals) can tell that these lights have been exchanged, the information must come from the other kind of cone pigment. Consequently, in measuring the exchange threshold in the protanomalous, we measure abnormal cones only.

The exchange light was presented superimposed on a red or green background. Backgrounds always raise the threshold (Weber's law) and we found the relative energies of red and green lights that raised those exchange thresholds equally. Now Stiles²⁻⁴ in his extensive studies of colour mechanisms in normal eyes, has shown that two background lights which for any mechanism raise the threshold equally are also equal in exciting that mechanism. We conclude that our red and green backgrounds were equal in exciting the abnormal pigment—the only one in operation at this exchange threshold.

With this information and Rayleigh matches (red+green) against not only yellow, but a set of monochromatic lights, it is possible to obtain the spectral sensitivity curve of the anomalous pigment. With our matching equipment (the Analytical Anomaloscope⁵) the answer is obtained directly.

The results are shown in Fig. 1 plotted as relative log spectral sensitivities in the red-green spectral range. Curve 1 is chlorolabe, present alone in the protanope, combined with 2 in the normal and with 3 in the protanomalous. Curve 2 is erythrolabe, present alone in the deuteranope, combined with 1 in the normal and with 4 in the deuteranomalous. Curve 3 is the anomalous pigment protanolabe, combined with 1 in the protanomalous. Curve 4 is the anomalous pigment deutanolabe combined with 2 in the deuteranomalous.

The combination 1 and 3 or 2 and 4 in the anomalous trichromat (instead of 1 and 2 in the normal) accounts for his abnormal colour matching, for the curves were obtained from these matchings. They also account for his poor colour discrimination. Clearly, the more nearly the two pigment curves coincide, the harder will it be for them to distinguish different wavelengths. Curve 4 lies close to 2, 3 even closer to 1, so these subjects have a very short "base" for wavelength discrimination. The similarity of their two pigments has also made it hard to separate these two pigments by retinal densitometry and other methods. But by accurately neutralizing the activity of the principal cones, we have been able to measure the spectral sensitivity of the others.

Piantanida and Sperling (private communication) have found these same pigments by entirely independent research. Measuring increment thresholds against critically selected backgrounds they appear to have been able to isolate the anomalous pigments. We are surprised that this was possible, but because they have found the same pigments that we found, they must be right.

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W. A. H. RUSHTON*
DIANE SPITZER POWELL
K. D. WHITE

*Institute of Molecular Biophysics,
The Florida State University,
Tallahassee, Florida*

Received January 16; revised February 16, 1973.

* Permanent address: Trinity College, Cambridge.

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Effect of Intravenous Prostaglandin $F_{2\alpha}$ on Small Intestinal Function in Man

ENDOGENOUS and exogenous prostaglandins (PGs) have been implicated in the pathogenesis of diarrhoea. $PGF_{2\alpha}$ may be secreted by some thyroid tumours which are accompanied by diarrhoea¹; when given for the termination of pregnancy this PG produces diarrhoea as an undesirable effect². Oral or intraluminal PGE_1 speeds up intestinal transit³ and causes secretion of fluid and electrolytes into the intestine⁴. In animals, PGE_1 and $PGF_{2\alpha}$ inhibit intestinal sodium transport⁵ and produce loss of fluid from intestinal loops⁶. Isolated human intestinal muscle responds to PGs with contractions or relaxations, depending on the site and the PG used⁷⁻¹⁰. In spite of these marked effects on both the secretory and motor functions of the gut, the action of intravenous prostaglandins on human small intestinal function has not been studied. We have measured the effect of intravenous infusions of $PGF_{2\alpha}$ on the net movement of water, electrolytes, transit rate and on pressure activity in the human jejunum and ileum.

Table 1 Mean Transit Time (min/30 cm of Intestine)

Study No.	Jejunum		Ileum	
	Control	$PGF_{2\alpha}$	Control	$PGF_{2\alpha}$
1	*	8.8	13.1	12.1
2	10.7	7.4	8.0	8.9
3	4.9	7.0	10.0	8.5
4	6.3	7.0	12.6	12.9
5	7.5	8.8	13.1	11.3
6	6.1	8.8		
7	7.9	9.5		
8	*	*		
9	8.1	14.5		

* Curve unsatisfactory.

Intestinal movements of water and electrolytes were measured in the jejunum of nine and in the ileum of six healthy male volunteers by means of a continuous steady state perfusion system using a triple-lumen tube¹¹. The position of the tube was confirmed radiologically immediately before the start of the perfusion. In the jejunal studies the infusion point was just distal to the duodeno-jejunal junction; in the ileal studies the infusion point was 65 cm proximal to the ileo-caecal sphincter. A 15 cm mixing segment and a 30 cm study segment were used; the infusion rate was 10 ml min⁻¹ in all except three studies (jejunal studies 1, 3, 5). Two additional lumens perfused with water at the rate of 10 ml h⁻¹ opened 5 cm apart in the study segment and were used to record intraluminal pressures. Transit through the study segment was measured with a dye injection technique¹² using 2 ml of phenol red (PSP) (6 mg ml⁻¹). The jejunum was perfused with a solution containing sodium and chloride 140 mmol l⁻¹ and mannitol 20 mmol l⁻¹; the ileum with a solution containing sodium 135, potassium 5, chloride 110, bicarbonate 30 and mannitol 20 mmol l⁻¹. Both solutions contained polyethylene glycol (PEG) 1 g l⁻¹ as an unabsorbable marker and were 300 mosM. Sodium chloride solution (0.9%) with or without $PGF_{2\alpha}$ was administered intravenously at a constant rate from a motor-driven syringe during the control and experimental periods respectively. Electrolytes and PSP were determined on an auto-analyser; PEG was estimated as described by Hyden¹³. Intraluminal pressure records were analysed in terms of the mean number of pressure peaks min⁻¹ recorded during each of the 10 min collection periods. A pressure peak was defined as a rise above the baseline of intraluminal pressure of 2 mm Hg or more. From the start of the intestinal perfusion at least 60 min were allowed for the development of a steady state. After equilibration, four-six consecutive 10 min collections were made to provide control data. The intravenous infusion

was then changed from saline to $PGF_{2\alpha}$ at the dose of 0.28–0.86 $\mu\text{g kg}^{-1} \text{ min}^{-1}$, and after a further equilibration period of 30 min, four 10 min collections were made. The doses of PG were similar to those used in therapeutic abortion. The results expressed are the mean values of the last three consecutive 10 min collections and pressure measurements during each period of study. Transit time was measured during the control and PG periods.

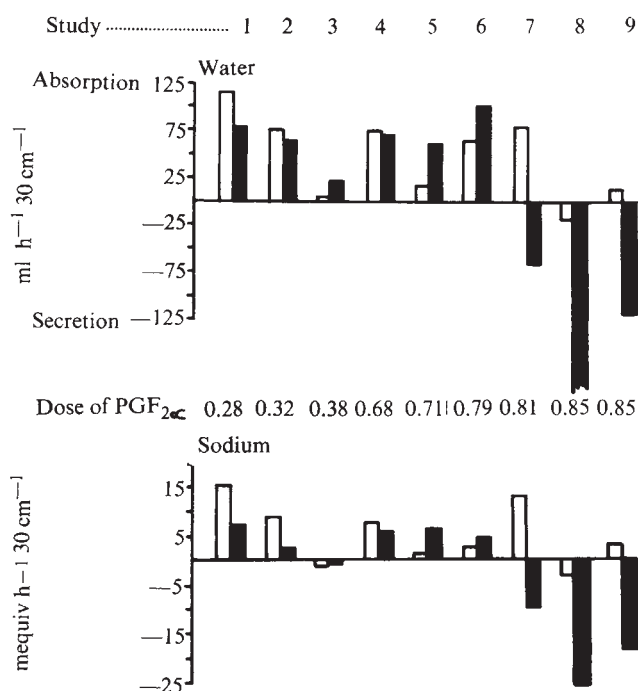


Fig. 1 Net water and sodium movements in the jejunum. Open blocks control, closed blocks $PGF_{2\alpha}$. Net absorption from the lumen above the line, net secretion into the lumen below the line. Mean values for the last 30 min in each study period are shown. Movements of chloride followed closely the movements of sodium.

In the jejunum net secretion of water, sodium and chloride into the lumen occurred in the three subjects receiving the highest doses of $PGF_{2\alpha}$ (0.81–0.85 $\mu\text{g kg}^{-1} \text{ min}^{-1}$). Net secretion did not occur until 30–40 min after the start of $PGF_{2\alpha}$ infusion. No change was observed in the remaining six who received doses of 0.28–0.79 $\mu\text{g kg}^{-1} \text{ min}^{-1}$ (Fig. 1). Satisfactory measurements of transit time were available in seven subjects and although some slowing occurred during $PGF_{2\alpha}$ infusion in six of these, the change was not statistically significant (Table 1). The frequency of the segmental pressure waves in the study segment was markedly diminished in the four subjects receiving the highest doses of $PGF_{2\alpha}$. The inhibition occurred within 10 min of the start of $PGF_{2\alpha}$ infusion and persisted to the end of the study (Table 2).

In the ileum net secretion of water, sodium and chloride into the lumen occurred in the four subjects receiving the highest doses of $PGF_{2\alpha}$ (0.65–0.86 $\mu\text{g kg}^{-1} \text{ min}^{-1}$), but no change was observed at the two lower doses (0.52 and 0.56 $\mu\text{g kg}^{-1} \text{ min}^{-1}$). In this respect the ileum appeared more sensitive than the jejunum, but the onset of net secretion was similarly delayed. Bicarbonate loss into the lumen was observed in three of the four subjects who secreted (Fig. 2). Measurements of transit time (available in five subjects) showed no consistent change during the administration of $PGF_{2\alpha}$ (Table 1). Pressure activity in the ileum was profoundly diminished in the five subjects given the highest doses (Table 2). Inhibition was rapid in onset and was sustained during the infusion of $PGF_{2\alpha}$.

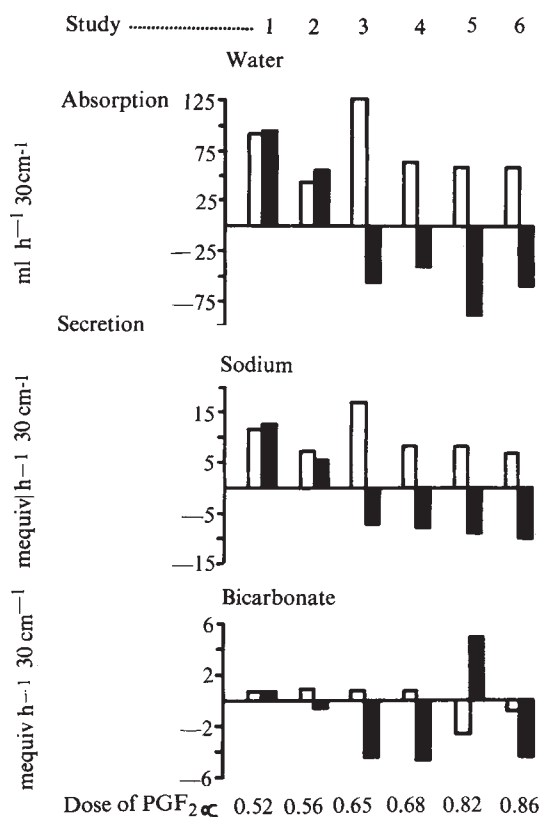


Fig. 2 Net water, sodium and bicarbonate movements in the ileum. Symbols as in Fig. 1. Movements of chloride followed closely the movements of sodium.

(Fig. 3). In four subjects (studies No. 3 to 6) progressive contractions (mean amplitude in proximal tip 50 mm Hg, in distal tip 38 mm Hg) were recorded during the infusion of PGF_{2α}, but their role in the propulsion of intestinal contents is uncertain.

During infusion of PGF_{2α} eight subjects experienced mild abdominal colic; this abdominal pain occurred in the presence of inhibition of small intestinal pressure activity. All but one of the subjects passed copious watery stools at the conclusion of the study. No changes were observed in pulse rates or blood pressures.

These results show clearly that intravenous PGF_{2α} profoundly affects the transport of water and electrolytes and the motor function of the small intestine, but it is uncertain which is more important in the pathogenesis of the diarrhoea. Both the jejunum and the ileum responded to PGF_{2α} by net secretion of fluid which was isotonic and approximated in composition to that normally found in these regions of the small intestine. Net movements of water and electrolytes into the intestine during infusion of PGF_{2α} were of a similar order to those observed in patients with cholera¹⁴ and diarrhoea caused by *E. coli*¹⁵. Our data do not enable us to speculate on the mechanism whereby PGF_{2α} exerts its effect on fluid movement

Table 2 Effect of PGF_{2α} on the Frequency of Segmental Pressure Waves

Study	Dose PGF _{2α} μg kg ⁻¹ min ⁻¹	Secre- tion	Motility: pressure peaks min ⁻¹		
			Control Last 30 min	During PGF _{2α} First 30 min	Last 30 min
Jejunum					
1	0.28	—	2.3	2.5	2.5
2	0.32	—	3.9	3.3	3.1
3	0.38	—	2.3	2.9	3.1
4	0.68	—	1.6	1.3	1.3
5	0.71	—	1.6	1.7	0.4
6	0.79	—	2.5	0.8	1.5
7	0.81	+	3.4	0.4	0.5
8	0.85	+	5.0	2.0	0.3
9*	0.85	+	—	—	—
Ileum					
1	0.52	—	3.2	2.8	2.5
2	0.56	—	2.1	0.6	0.8
3	0.65	+	4.6	2.0	2.7
4	0.68	+	3.6	1.6	2.0
5	0.82	+	2.9	1.1	0.7
6	0.86	+	5.0	1.1	1.3

* Pressure record was technically unsatisfactory in jejunal study No. 9.

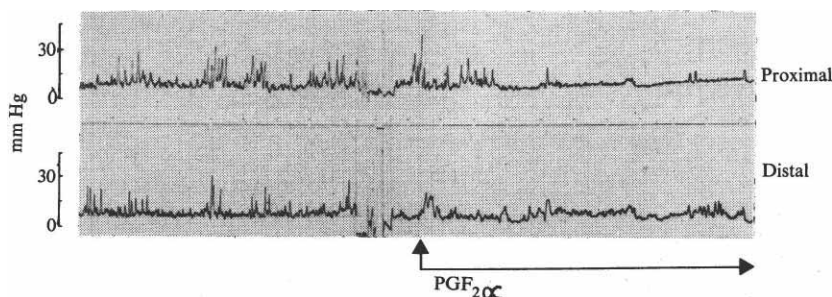
in the intestine. Net secretion did not, however, occur until 30–40 min after the start of PGF_{2α} infusion. This delay may be due to a rise in the concentration of circulating PGF_{2α} or active metabolites, but may also be explained by PGF_{2α} requiring a second messenger system to exert its effect.

Inhibition of small intestinal segmental pressure activity occurred sooner and at lower doses than the production of net fluid secretion into the lumen, suggesting a different mode of action by the PGF_{2α} on the muscle of the small intestine. This inhibition of motor activity may have been due to relaxation of the circular muscle. The circular muscle of the human ileum is inhibited *in vitro* by PGE₁ and E₂ (ref. 8). Our recording system did not allow us to measure changes in the activity of the longitudinal muscle layer, which *in vitro* is contracted by PGE₁, E₂ (ref. 8) and F_{2α} (ref. 9).

Propulsion of intestinal contents may be facilitated by inhibition of segmental pressures. Low segmental pressure activity has not been previously described in the small intestine during diarrhoea, although it occurs in the colon¹⁶. In spite of the diarrhoea, we were unable to record significant changes in transit time. On the other hand, the flow in the test segment increased by a mean of 1.46 ml min⁻¹ in the jejunal, and by 1.26 ml min⁻¹ in the ileal studies, in which secretion occurred: this represents an increase of some 15% above the rates of flow during the control period.

The presence of colic in spite of inhibition of small intestinal segmental pressures suggests that the colon may also be responding to infused prostaglandin: contractions of isolated human colonic muscle to PGF_{2α} have been reported¹⁰. Alternatively the colic and diarrhoea could result from the entry of a large volume of fluid into the caecum, with subsequent mass-movements and rapid propulsion of colonic contents.

Fig. 3 Pressure activity in the ileum before and during PGF_{2α} infusion. Top trace proximal, bottom trace distal open-ended tube. Time marker, 1 min.



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J. H. CUMMINGS
A. NEWMAN
J. J. MISIEWICZ

Medical Research Council,
Gastroenterology Unit,
Central Middlesex Hospital,
London NW10 7NS

G. J. MILTON-THOMPSON
J. A. BILLINGS

The Royal Naval Hospital,
Haslar,
Gosport,
Hampshire

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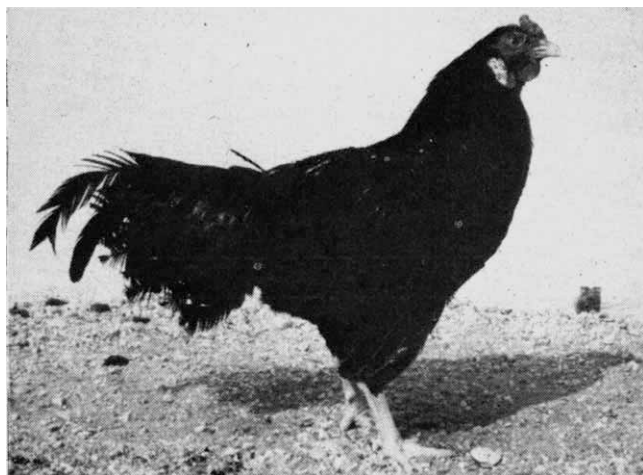


Fig. 1 Adult diploid parthenogenetic rooster.

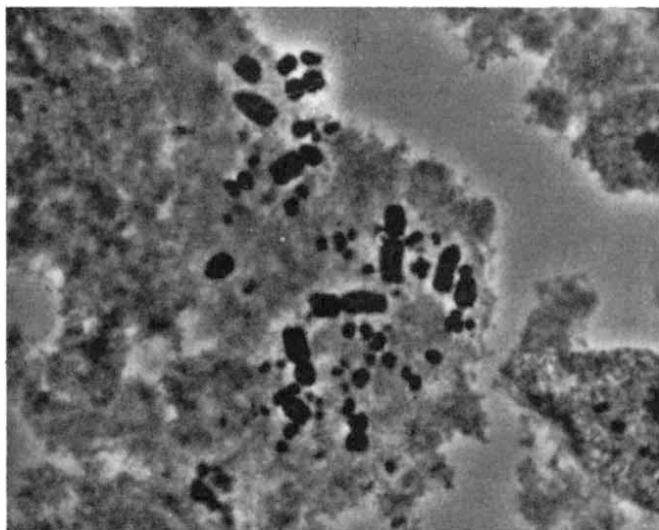


Fig. 2 Diploid cell from a parthenogenetic embryo. Note the ZZ chromosomes.

Adult Parthenogenetic Chickens

PARTHENOGENETIC chickens have been reported as embryos or chicks that lived to a maximum of eight days¹⁻³, except for one triploid White Leghorn chicken⁴. This chicken was from a virgin White Leghorn hen being tested as a control for a Dark Cornish-type stock which was under genetic selection for a high rate of parthenogenetic development. A cytogenetic study is in progress to determine the origin of parthenogenesis and to obtain parthenogenetic chickens.

In 1972, four parthenogenetic chicks were hatched from 8,532 eggs of the Dark Cornish-type stock⁵ and raised to maturity. Three other chicks were hatched, but died during the first week. Average time to hatching was 24.4 days. These eggs were laid by virgin hens, sexed at six weeks of age and placed in separate pens. When the hens neared reproductive age they were placed in individual cages. No males were kept in the same room as the virgin hens. Special care had to be given to these chicks because they seemed to die as a result of gaseous inflated intestines, suggestive of enterotoxaemia. Therefore, as soon as the chicks started to pip the holes were enlarged and they were fed orally a mixture of 2,000 units of penicillin and 1 mg streptomycin each day for three days. The chicks were allowed to hatch normally the next day or were helped out of the eggs if they had difficulty. Some chicks had to be hand fed for the first two or three days. After this time, they were strong enough to feed themselves.

Four Dark Cornish-type chickens (Fig. 1) survived this treatment, and reached maturity. These birds are males and one mated with a White Leghorn female to produce fertile eggs. Chromosome counts from the feather pulp showed this male was diploid. Two of the other birds are also diploid. Fig. 2 shows a somatic cell from a colchicine-treated parthenogenetic embryo. The hen that laid this egg also laid an egg giving rise to one of the parthenogenetic roosters. The cell is diploid, and both ZZ chromosomes are present as they were in the parthenogenetic roosters that were raised. These are the first examples of adult diploid parthenogenetic chickens.

PATRICIA SARVELLA

Animal Physiology and Genetics Institute,
Agricultural Research Center,
Agricultural Research Service, USDA,
Beltsville, Maryland 20705

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Elimination Kinetics of α -Amino-iso-butyric Acid in Non-Pregnant and Pregnant Rabbits

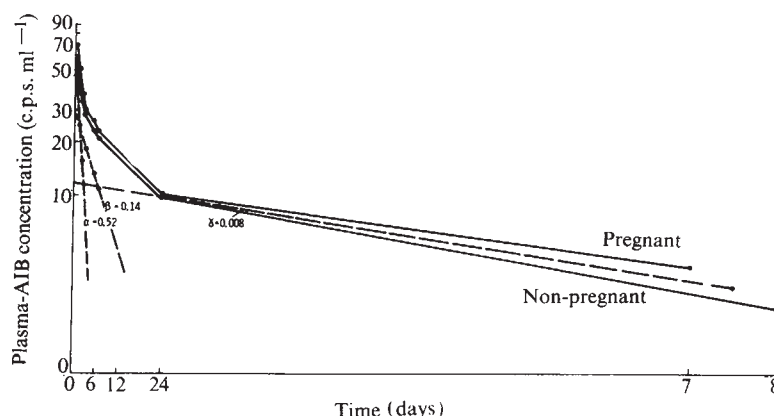
CHANGES in the maternal metabolic and excretory functions occur during pregnancy; the plasma elimination rates of many compounds, such as folic acid^{1,2}, cortisol³⁻⁵, nalidixic acid or gentamycin⁶, have been found to differ in non-pregnant and pregnant subjects. Also, the plasma steady state concentration of most of the free amino acids is already lowered early in pregnancy. Here I report on the elimination rate of the model α -amino-iso-butyric acid (AIB) in pregnant and non-pregnant rabbits. I chose this amino acid because it is not metabolized^{7,8}; it is transported and distributed throughout the body by the same mechanism as the naturally occurring

The elimination curve of ^3H -AIB does not seem to be linear on the semilogarithmic scale and therefore first order kinetics are not applicable for the characterization of the disappearance of this substance from the plasma of non-pregnant and pregnant rabbits. It is, however, possible to show¹⁴ that the experimentally obtained data closely fit a third order elimination model represented by

$$y = C_1 e^{-\alpha t} + C_2 e^{-\beta t} + C_3 e^{-\gamma t}$$

where the elimination constants are $\alpha = 0.52$, $\beta = 0.14$, $\gamma = 0.008$. Because I assume that the metabolic and excretory functions of the animals do not change during the periods of experiment, this indicates that the elimination of ^3H -AIB is determined simultaneously by the kinetic properties of three different compartments.

Fig. 1 Plasma elimination curve of ^3H -AIB in rabbits.



free amino acids preferring the A-mediating system^{9,10}; it is slowly and almost exclusively excreted by the kidneys^{7,8,11}; and it is believed to accumulate in fast growing foetal tissue^{12,13}. Twenty-one experiments were performed using nine rabbits. Ten experiments were carried out in the non-pregnant and eleven in the pregnant animal. The pregnant rabbits were investigated in the first and third weeks of gestation.

A single dose of tritiated AIB (^3H -AIB, specific activity 1.8 Ci mmol^{-1}) was administered intravenously. Blood samples were then drawn from the ear vein after 30, 70, 130, 180, 310 and 400 min. Two additional samples were collected after ~24 h and 1 week. The plasma ^3H -AIB concentration was measured in a Packard Tricarb Scintillation Counter.

Table 1 Plasma ^3H -AIB Concentrations at Different Times after Injection of a Single Dose (45 μCi) into Non-Pregnant and Pregnant Rabbits

Time after injection (min)	³ H-AIB concentration (c.p.s. ml ⁻¹) (mean ± s.e.)	
	Non-pregnant (n=8)	Pregnant (n=4)
30	57.2 ± 2.9	68.7 ± 5.8
70	42.2 ± 3.0	51.1 ± 9.1
130	33.9 ± 2.1	37.6 ± 3.8
180	28.9 ± 1.8	30.9 ± 2.6
310	23.2 ± 1.6	26.6 ± 2.4
400	21.3 ± 1.4	23.0 ± 2.2
24 h	9.8 ± 1.2 (n=10)	10.3 ± 0.7 (n=11)

Table 1 and Fig. 1 summarize my results. In the pregnant rabbits the plasma concentrations are generally higher and the elimination slightly slower than in the non-pregnant. There is, however, no statistically significant difference between the two groups of animals, and the results for the different stages of pregnancy are also similar.

Henriques *et al.*¹⁵, measuring the elimination rate of the naturally occurring free amino acid glycine in non-pregnant rabbits, came to similar conclusions. They were unable to find a single value for the plasma half-life of glycine and also suggested that at least three body compartments have an influence on the elimination kinetics of this particular amino acid.

FELIX KRAUER

Department of Gynaecology,
St Thomas's Hospital Medical School,
London SE1

Received December 12, 1972.

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BOOK REVIEWS

Agriculture Under the Weather

Times of Feast, Times of Famine: a History of Climate since the Year 1000. By Emmanuel Le Roy Ladurie. Pp. xvi+428. Translated by Barbara Bray. (George Allen and Unwin: London, January 1972.) £7.35.

It was in the late 1950s that the author of this book, then a young French economic historian engaged in research on the agricultural history of the sixteenth and seventeenth centuries in the Languedoc in the south of France, found it necessary to construct a history of the climate to explain his data. At the same time he found that the archives and documents he was using were extremely rich in weather data: for the peasants recording the poor harvests, famines, shortages and occasional years of abundance, had been intimately aware of the way in which their troubles were associated with the climatic stress of those times. Le Roy Ladurie's career over the years since has been a story of the enthusiasm and apparently boundless energy with which one historian, ignoring the alleged gulf between the two cultures of letters and science, applied himself to mastering all sources of information about past climate. The references in this book include the most relevant works in French, English, German, Russian and other languages besides, not only on local and regional history and archaeology, but also on vintages and tree growth and their climatic correlations, on pollen analysis, vegetation history and radiocarbon dating, the variations of the glaciers in Europe, Africa, America and the Arctic, and the blooming dates of the cherry in Japan, the variations of lakes in America and the Soviet Union as well as texts in hydrology, meteorology and oceanography. This praiseworthy effort has produced not only a realistic history of the environment, the background to human history which is still far too dimly perceived (if at all) by most human historians outside Scandinavia; it is also a book that is as charming, and appropriately illustrated, as it is informative.

Nor is this book only of academic importance in the unravelling and better

understanding of the past. Scientists, too, who are confronted with the embarrassing demand for 50-year forecasts of the future trend of climate, need such reconstructions of the past record as Professor Ladurie has provided as the basic material of their studies. There can be no theoretical modelling of the long-term processes of climate without data. And for this purpose this book furnishes some tables of unusual length and completeness.

In detail, the book starts with the historical study of climate, this theme being expanded in chapter 2 by a consideration of the climatological evidence derived from tree growth (tree rings) and wine harvests. Two further chapters deal with the recent "amelioration" of climate over the half century ending about 1940, and with the problems of the "little ice age" between 1560 and about 1860, when glacier advances at least in the Alps were most spectacular and responsible for human distress around 1600, 1643-44, 1820, and 1850. A chapter follows on "working hypotheses" in which the available evidence from documents, instrumental records, and from wine harvest dates, tree-ring widths and so on, are synthesized and correlated with the observed climatic fluctuation over the past four centuries. A reconstruction of mediaeval climate from documents and from records of the Norse voyages to Greenland, radiocarbon dating of trees overwhelmed by glacier advances, oxygen isotope ratios in a deep core taken from the Greenland ice cap, phenological records and dates of the freezing of rivers receives a chapter to itself. All this leads to a final chapter on the physical causes and human consequences of climatic fluctuations.

From the start Professor Ladurie avoids the pitfalls inherent in the climatic interpretation of history followed by some of his predecessors. For example, wheat, wine and hay receipts for the estates of the Abbey of St Denis (Paris) were "steady as a gyroscope between 1284 and 1342". (Evidently the extreme wetness of the years 1313-

1317 affected France much less than the rest of Europe.) Then the graphs of these receipts went "hurtling downward" after 1346-1348 because of the plague, the English and the brigands. Similar non-meteorological hazards ravaged the agriculture of north-eastern France during the same period. His analyses of the social and economic factors involved in addition to climatic conditions, in French wine growers choice of harvesting dates; besides his detailed descriptions of outstandingly cold epochs in France such as 1617-1650, with its critical glacial advances in the Alps in 1643-1644, are comprehensive and scholarly, and the book abounds with many other fascinating and illuminating examples of this sort. In justification for his detailed history of the "little ice age" he explains that earlier workers in this field have been scientists or geographers but not historians. Even writers "as reputable and competent as C. E. P. Brooks, coming from a country without glaciers . . . have fictionalized their "little ice age"; hence Professor Ladurie has worked in decades rather than centuries or longer.

A few minor criticisms can be made. On page 64, and occasionally on other pages, monthly climatological data make tedious reading and might have made more impact in tabular form. The author writes of "foggy wet summers" on page 74; probably a literal use of the source description. On pages 302 and 304 the word "meridian" should have been translated as "meridional", its English equivalent. Occasionally a diagram suffers in reproduction, Fig. 2 is one example, but in general the plates are beautifully reproduced and admirably supplement the text.

There is much evidence that the author has brought his work right up to date. For example, the dendro-chronological work done at Tucson, Oxford and Caen is discussed (pages 40-42). He makes a vigorous plea (page 287) for more thorough collection and classification of vast numbers of scattered climatic references by computerization. Elated by the agreement

he derives between wine harvest dates and glacier movements (page 79), he hopes that "young researchers in France, Hungary or Switzerland will work out the same sort of chronology on wine quantity for their own countries as Müller has provided for Germany".

The actual change in air temperature (about 1°C) between the little ice age and the recent "amelioration" in England, which seems small to the layman, makes about a month's difference to the length of the growing season. Both this and the cooling which has set in during the last two decades receive careful attention in Professor Ladurie's book, along with its pleasing production and printing.

R. F. M. HAY
H. H. LAMB

Excavation Under Water

Underwater Archeology: a Nascent Discipline. (Monuments and Museums, XIII.) Pp. 306. (Unesco: Paris, 1972.) 44 francs; \$11; £3.30.

THIS book is in some respects aptly titled: underwater archaeology is a discipline which to a large extent is (as a dictionary defines "nascent") "in the act of being born, not yet mature". But it is misleading to apply a blanket description to so wide-ranging a subject, for, as the book clearly shows, some of the results so far obtained have been markedly less immature than others. For this reason it is particularly useful to find that the wide spectrum of results summarized here have been, in the main, chronicled by their various progenitors. The work of Professor Bass and his Pennsylvania University colleagues on ancient shipwrecks in the eastern Mediterranean bears comparison with the most exacting archaeological standards in or out of the water—as Bass himself stresses it should do. Likewise the well-known *Wasa* salvage, the excavation of wrecks from the drained polders of the Zuider Zee, the recovery of the Skuldelev viking ships from Roskilde Fjord, the Bremen Cog excavation, the work on ancient harbours and other submerged sites in the Mediterranean and elsewhere, and the fascinatingly precise sectioning of prehistoric remains in the Lake of Zurich, all weigh heavily on the credit side of the archaeological balance.

On the debit side, however, much work carried out over the past two decades on early wrecks on the eastern seaboard of the Americas seems to have been disturbingly inadequate and destructive, doubtless because privately sponsored treasure hunting appears to have been the primary motivation behind their discovery and excavation. Although structural remains of vessels dating back to the sixteenth century have been found there in some profu-

sion, thus potentially covering an important and ill-documented period in the development of shipbuilding technology, Peterson's chapter gives no indication either in text or references of the existence of any published plans of such remains. To some extent the same criticism could be levelled at a good deal of what has been going on in our own waters, though the book, rather surprisingly, makes no mention of British work. It is worth reflecting that a close relationship exists between the quality of results achieved in a particular country and its government's degree of constructive involvement in this field: it is no coincidence that to date such involvement has been, both in the United States and in Britain, almost negligible.

The book includes useful chapters on techniques, not all of which, however, are wholly up to date. Williams's chapter on photogrammetric survey is practical and good, but Townsend's review of conservation procedures is less adequate, and—in common with the two other conservation chapters—does not mention important recent improvements in the treatment of waterlogged wood.

There is much in this book which is good, though a substantial amount is bad and more still is indifferent. This accurately mirrors the varying standards to be found within this new discipline as it endures its birth-pangs, and the book as a whole thus provides a useful survey of how the subject stands at present and where its strengths and weaknesses lie. As its editors themselves point out, it is a status report and not a textbook.

COLIN J. M. MARTIN

Applied Relativity

Gravitation and Cosmology: Principles and Applications of the General Theory of Relativity. By Steven Weinberg. Pp. xxviii+657. (John Wiley: New York and London, September 1972.) £8.

IN the last twenty years general relativity has developed dramatically in two opposite directions. On the one hand more powerful mathematical methods have clarified the general structure and significance of the theory, while on the other it has come into close contact with modern astrophysics. Put crudely, but not altogether inaccurately, we now have two subjects: topological relativity and engineering relativity. This book is unashamedly about engineering relativity. It is written by a man well known for his brilliant contributions to the theory of elementary particles, and for his occasional forays into relativistic astrophysics. In my opinion the book is quite superb as an introduction to its subject.

It begins with a brief, physically oriented, account of special and general relativity in sufficient mathematical detail for the later astrophysical applications. These applications begin with a treatment of stellar equilibrium and collapse. The level of this treatment is that of an introductory survey rather than a comprehensive account of the kind that can be found in Zeldovich and Novikov's book *Relativistic Astrophysics* or in various summer school lecture notes by Thorne. Nevertheless I would recommend it as an excellent introduction to the more detailed treatments. The book then reverts to a consideration of some mathematical developments used in general relativity, namely, concerning the action principle, the tetrad formalism and space-times which possess symmetries. It is not clear to me why this material is inserted into the middle of the astrophysical part of the book, rather than in the chapters on general relativity. It is true that the discussion of symmetries is of basic importance for the following section on cosmology, but it is also needed for the derivation of the Schwarzschild solution, where indeed a forward reference has to be made.

Finally we come to the cosmology section, which occupies the last two hundred or so pages of the book. The treatment here is up to date and has a physical orientation which I found very satisfying. Of particular value are the sections on intergalactic emission and absorption processes, the cosmic microwave radiation background, the thermal history of the early universe, and the formation of galaxies. In the final chapter there is a brief account of non-standard models of the universe which includes relativistic models with a cosmical constant, the steady state theory, and models with a varying constant of gravitation.

The book as a whole is clearly written, is pervaded by physical insight, and contains sufficient mathematical development to serve as an introduction to more detailed treatments and to the original literature. I recommend it to all physicists who want to gain a serious understanding of modern relativistic astrophysics, to students who wish to start work in this subject, and even to my colleagues.

I have left myself enough space to air one small quarrel which I have with the author. It concerns his attitude to the principle of equivalence and to Mach's principle. In the preface he states that the reason why gravitation obeys the equivalence principle is not to be found in classical physics but in the constraints imposed by the quantum theory of gravitation. In the body of the book he states that there is a sense in which the equivalence principle and Mach's principle are in direct opposi-

tion. I disagree with both these statements. Indeed I believe that Mach's principle precisely gives us the reason why gravitation does obey the equivalence principle, because it is the gravitational force of the distant accelerating masses which we interpret, with Mach, as an inertial force, and it is to be expected that the effects of this gravitational force on a physical system are fully equivalent to those of a (uniform) gravitational force of local origin. This conceptual question does not intrude elsewhere in the book, however, and I hope that it is widely read.

D. W. SCIAMA

Primate Anatomy

Evolutionary Biology of the Primates. By W. C. Osman Hill. Pp. x+233. (Academic: London and New York, December 1972.) £3.90.

THROUGH his monographic series, *Primates, Comparative Anatomy and Taxonomy*¹, W. C. Osman Hill has already performed a great service to primatologists by providing a basic reference source. However, there must be many who have hoped that he would also find time to write a short synthetic text for students, summarizing developments in the field of comparative anatomy since 1954 (the date of publication of his introductory text *Man's Ancestry*²). *Evolutionary Biology of the Primates* fills this gap with a succinct new review of Hill's encyclopaedic knowledge of primate anatomy. The book is based on a course of lectures designed for the NATO Advanced Study Institute on Comparative Biology of Primates, which was held in Turin in June 1972. Since the course was specifically designed for the training of primatology students, this is obviously the kind of book that one should consider for university teaching of primate anatomy and evolution, and it is inevitable that it will be compared with Le Gros Clark's *Antecedents of Man*³, which has served as a basic text in this area for many years.

Hill's new book resembles that of Le Gros Clark in that it deals with primate anatomy in terms of separate organ systems. Indeed, a fair number of illustrations have been republished from *Antecedents of Man*. There is also the same heavy reliance on the structure of the skull and brain. However, Hill's approach differs in that, although the evolution of organ systems is considered in terms of different levels ("phases") of organization exhibited by living forms, the apparent linearity of this treatment is offset by separate discussion of the evolutionary radiation of the individual major groups of primates. A further significant advantage lies in the inclu-

sion of a general section on the radioprimate evolution in its proper perspective of the placental mammals, placing it — a perspective which is far too readily forgotten in many modern primatological studies. Thus, although *Evolutionary Biology of the Primates* and *Antecedents of Man* share many features of structure and content, there are enough differences to justify coexistence of the two texts as complementary aids to the study of primate anatomy. Hill's book is also more up-to-date in a number of respects.

It would have been better, however, to entitle this new book "*Comparative Anatomy of the Primates*". There is no real discussion of evolutionary biology at any point, and there is very little reference to behaviour, physiology or biochemistry; in short, there is little mention of function. For example, the section on "Diet and Digestion" is almost exclusively concerned with the anatomy of the digestive tract, and not with function or the functional background to evolution. The only evolutionary model that is used in the text is that of the "phylogenetic scale", and Fig. 14 (page 19) shows "a series comprised of some living species arranged in an ascending evolutionary order". Although Hill points out that this "series" should not be taken literally, it does in fact form the primary basis for evolutionary inference throughout the book, for instance in the discussion of the evolution of the brain in terms of "phases" represented among living primates. The use of the phylogenetic scale concept is also prominent in the section on the placenta. Although it must be recognized that this scale concept has played a vital role in the development of primate evolutionary theory, its limitations should not pass unremarked^{4,5}. In any event, many workers would question the implication (Fig. 14) that the orang-utan is more closely related to man than is the gorilla!

In view of the concentration on brain anatomy, it is unfortunate that there is no discussion of primate brain: body weight ratios, and no mention of the meticulous work carried out in this area by Stephan and Bauchot⁶ over the last decade. The only reference to relative brain size is contained in a table (page 38) which misleadingly repeats individual measurements from 3 species, in one case derived from an apparently juvenile tree-shrew! In view of the evolutionary interest, it is also a pity that there is no mention of endocranial casts from fossil primates, since this provides the only direct evidence of brain evolution^{7,8}. Finally, there is no mention of recent work on the primate retina, such as that of Wolin and Massopust⁹. These are all important omissions, and similar gaps occur in other parts of the book. For example, it is surprising that

only 1½ pages are devoted to the key fossil primates of the Fayum, whilst less important fossils receive more detailed examination.

Thus, it must be recognized that this book has severe limitations as a basic text on primate evolution. Within the confines of these limitations, however, one is presented with a competent and well-illustrated text which is generally admirable in its clarity. The section on dental morphology in primates (pages 75–87), for example, is a model of clear explanation from first principles. Given the fact that this book also has a very reasonable price, it obviously has a broad appeal as a basic text in primate anatomy, and it should certainly be recommended to students as introductory reading, along with books covering other aspects of primate biology.

R. D. MARTIN

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Atmospheric Science

An Introduction to Air Chemistry. By S. S. Butcher and R. J. Charlson. Pp. xiii+241. (Academic: New York and London, November 1972.) \$10.95.

THE contents of this book evolved from a set of class notes used by the authors in teaching. It is intended that the book be used by those with no previous experience in the field of atmospheric sciences as an introduction to the study of the chemistry and meteorology of the atmosphere. As its origins and title suggest, the book is set at the undergraduate level of study and as a textbook to accompany a lecture course it will be useful to both students and lecturers. The text is clear and presented in a way which will attract and retain students' interest. The authors

usually appreciate that after an introduction many will need to go on to more detailed treatments and the necessary references and suggestions for further reading are included. In any textbook which attempts to bring together relevant aspects of meteorology, physics and chemistry the choice of material must inevitably be arbitrary and some readers will find the book contains less chemistry and rather more physics and meteorology than they might have expected. The title is, in fact, somewhat misleading and would be improved if the word "chemistry" in it were changed to "science".

The authors' claim that the book could be used as a reference text by workers in atmospheric chemistry is rather optimistic and at variance with the aims and achievement of what is essentially an introductory course. Similarly the use of the text by research workers new to the field of atmospheric science will be limited to the acquisition of a useful introduction and an indication of where more detailed treatments may be found.

The usefulness of some of the early chapters of the book as a text for teaching will depend to a large extent on the student's experience. The study of atmospheric science would probably fit best into the later stages of an undergraduate course and the summary of chemical principles in chapter 2 may well have been covered in much greater (and necessary) detail by that stage. The modern student would probably appreciate more detailed treatment of topics of contemporary interest such as heavy metals, halogens and the upper atmosphere, and the authors should consider their inclusion in future editions of this useful introductory text.

W. S. CLOUGH

¹³C Spectroscopy

Carbon-13 NMR Spectroscopy. By J. B. Stothers. Pp. xi+559. (Academic: New York and London, November 1972.) \$24.

THIS book, written by an author who is well known for his ¹³C n.m.r. work, is intended for organic chemists and others of graduate and research worker levels. Because the full potential of the ¹³C n.m.r. techniques are just beginning to be exploited this book makes a timely and welcome appearance. Fourier transform n.m.r. spectrometers which are particularly useful for ¹³C n.m.r. studies are now commercially available.

The book starts off with a short introductory chapter on the underlying theory and also makes a useful comparison with the well known proton method.

This is followed by part 1, the first of four self-contained parts which consists of a chapter on the experimental measurement of ¹³C parameters by both direct and indirect methods, and a discussion of their advantages and limitations is given. The statement that "pulse techniques will no doubt become popular" (page 19) seems to date the book somewhat. This no doubt reflects the surge forward in n.m.r. instrumentation during the time lapse which has occurred between writing and publication of the book.

The main part, part 2 (six chapters) consists of an extremely useful and comprehensive survey of ¹³C n.m.r. shielding data covering the literature to mid-1970 in which all the shieldings are given relative to tetramethylsilane (with increasing positive numbers to lower fields). Data are presented for hydrocarbons and substituted hydrocarbons, organometallic compounds, carbonium ions, heterocyclic systems, carbonyl carbons and nitriles. In addition the current theoretical interpretations of the trends observed are discussed. This section helps to pinpoint those areas in which much further ¹³C shielding data is required (for example for organometallic, sulphur and silicon compounds).

Part 3 (two chapters) considers the experimental determination together with the theoretical aspects of ¹³C spin-spin coupling constants. A survey of mainly ¹³C-H; ¹³C-¹⁹F and ¹³C-¹³C interactions is given which is not claimed to be comprehensive, because as the author rightly points out, the literature of even one bond ¹³C couplings is enormous. More emphasis is placed on interactions over two or more bonds.

Part 4 (one chapter) consists almost entirely of examples using direct observation of ¹³C spectra so as to illustrate the present usefulness and the potential scope of this technique. Structural elucidations together with stereochemical assignments dealing with geometrical isomerism and conformational analysis are first considered, followed by applications involving natural products illustrated with examples from the terpene, steroid, carbohydrate, nucleoside, nucleotide, amino-acid and peptide fields. Some applications involving polymers and petroleum are also given. Finally, the use of ¹³C tracer techniques for the study of reaction-mechanisms and biosynthetic pathways and for solute-solvent interactions are discussed.

The book, which is well written and readable, contains in addition to the usual author and subject index, a useful compound index to shielding values and/or coupling constants given in the text. No research worker in the field can afford to be without this book on his laboratory shelf and I strongly recommend it to anyone interested in ¹³C spectroscopy.

R. G. REES

Internal Friction

Internal Friction of Structural Defects in Crystalline Solids. By R. De Batist. Pp. xii+477. (North-Holland: Amsterdam and London; Elsevier: New York, 1972.) Dfl. 120; \$37.50.

A VAST amount of information about the internal friction and associated properties of metals and other crystalline solids has been published during the past twenty years. This material has been reviewed in the series *Physical Acoustics*, edited by W. P. Mason, but that series contains many volumes and René De Batist correctly appreciated that there was a need for a single volume covering the techniques of internal friction measurements and their application to the study of lattice defects in crystalline solids.

The opening chapter surveys the basic properties of various structural defects; point defects and dislocations are considered in some detail while grain boundaries, domain boundaries and three-dimensional defects are briefly mentioned. Chapter 2 contains a formal description of anelasticity and a detailed discussion of relaxation phenomena, and concludes by describing a useful selection of the many different experimental techniques which have been used for measuring internal friction.

The remaining three chapters are concerned with internal friction caused by point defects, dislocations and two-dimensional defects respectively. In each case the author gives a comprehensive survey of the experimental data; this review of the experimental results is one of the most valuable features of the book. The theory of the relaxation of point defects, which is now fairly well established, is described clearly and in detail. By contrast, I was disappointed to find that recent modifications of Seeger's theory of the Bordoni peak are mentioned only briefly and qualitatively. The vibrating string model of dislocation resonance is discussed in detail, and there are useful sections on the various interaction effects between dislocations and point defects and on the application of internal friction techniques to the study of radiation damage in solids.

This book serves a valuable purpose in linking together in one volume the many aspects of internal friction which are often considered in isolation. The author has himself made valuable contributions in a range of different topics, and his experience has enabled him to select his material successfully and to discuss it in an authoritative manner. The book is well produced, with only a relatively small number of typographical errors, but it is a pity that its price is such that it may not reach the desks of all the research workers who might benefit from it. D. H. NIBLETT

CORRESPONDENCE

Princeton in Trouble

SIR,—I think that your editorial "Princeton in Trouble" (*Nature*, **242**, 217; 1973) is highly damaging to the Institute of Advanced Study and the world of science in general.

First, I would point out the absurdity of the notion of social science. Science, as we all should know, consists foremost, of the application of the scientific method to the observation of natural phenomena. One of the essential requirements of scientific analysis is that it be possible to construct controlled experiments. In social studies of human beings, there is no possibility of constructing controlled experiments. Those who consider such a possibility should be strongly opposed. The second important requirement is that the experiments be repeatable. Since social situations are unique and cannot be repeated, social studies fail to meet the requirements of science on both counts. I would like to bring to your attention an excellent description of science in *Science is God*, by David F. Horrobin.

Next your suggestion "that there should be a better sense of moderation in this kind of scientific community" is immoral. If the standards of excellence and intellectual integrity are not maintained in such an academic community, then it is hard to conceive of any other place in the world where they would survive.

Your comment that "it is absurd for anybody at Princeton to suggest that a single appointment can entirely change the character of the faculty" is unfortunate and disputable. It is only single individuals that have been responsible for the course of human intellectual endeavour, to wit Socrates, Newton and Einstein.

Your comment that the dissident members' arguments are pernicious (the dictionary meaning of pernicious: extremely hurtful; wicked or mischievous) is slanderous. The faculty at Princeton does not possess such low qualities as you seem to do. It is editorials such as yours, and not their faculties that damage renowned institutions like the Institute of Advanced Study.

Yours faithfully,

S. MARATHE

Rice University,
Houston, Texas,
77001

β -Carotene

SIR,—In response to McDonagh's answer (*Nature*, **241**, 151; 1973) to our earlier communication (*Nature*, **240**, 59; 1972), we offer the following comments.

In the interests of brevity, we did not belabour the distinction between topical and systemic administration of carotene. Since the scope of the discussion has now been broadened, it should be noted that Kesten made the logical progression from validating the efficacy of topical carotene, to oral administration of the compound, and that although exposure of the untreated patient's skin to a 'Mazda' projection bulb produced a wheal, the response could not be elicited after two weeks of oral therapy.

Admittedly, Kesten did not have the benefit of our present knowledge of the aetiology of erythropoietic protoporphyria (EPP), the *in vitro* photosensitizing action of protoporphyrin via singlet oxygen, and the quenching ability of β -carotene. But, despite convincing "test tube" evidence, there appears to be no experimental data relating to the *in vivo* state in humans¹. McDonagh cited no evidence in support of his statement that the protective effect of β -carotene is enhanced when taken internally, and that the compound probably acts as an *in vivo* quencher of singlet oxygen as well as a light shield. On the contrary, the meagre information available suggests that oral β -carotene acts mainly (if not solely) as a screen to absorb harmful rays of the Sun, in a manner analogous to that of topically applied material. Thus, oral carotene does not provide photoprotection in EPP patients until serum concentrations reach massive levels² and the skin displays visible evidence of the presence of the carotenoid¹, which suggests to us that its mechanism of action is primarily that of a physical sunscreen. This conclusion is strengthened by the well-known observations that internally-administered carotene accumulates in the stratum corneum³.

It is unfortunate that the *in vivo* protective action of β -carotene is not strongly enhanced by quenching; the EPP patient whose situation is desperate enough to require massive carotene loading must pay the penalty of an unesthetic yellow colour in his skin. We have successfully treated EPP⁴ and other types of photosensitivity⁵ with topical application of dihydroxyacetone and

lawsone (2-hydroxy-1,4-naphthoquinone). This combination exhibits the property, shared by no other sunscreen, of binding chemically to the skin, and therefore does not require renewal during the patient's normal daily activities. The colour imparted to the skin is pleasing to the patients, and far more esthetic than the yellow hue of β -carotene.

Yours faithfully,

J. A. JOHNSON

R. M. FUSARO

University of Nebraska Medical Center,
Omaha, Nebraska 68105

¹ Mathews-Roth, M. M., Pathak, M. A., Fitzpatrick, T. B., Harber, L. C., and Kass, E. H., *New Eng. J. Med.*, **282**, 1231 (1970).

² Fitzpatrick, T. B., Pathak, M. A., Parrish, J. A., and Mathews-Roth, M., *Proc. Roy. Soc. Med.*, **64**, 861 (1971).

³ Ormsby, O. S., and Montgomery, H., *Diseases of the Skin*, 716 (Lea and Febiger, Philadelphia, 1954).

⁴ Fusaro, R. M., and Runge, W. J., *Brit. Med. J.*, **1**, 730 (1970).

⁵ Fusaro, R. M., Runge, W. J., and Johnson, J. A., *Intern. J. Dermatol.*, **11**, 67 (1972).

Ancient Egypt

SIR,—With regard to the recent paper by K. H. Hsu *et al.* (*Nature*, **242**, 240; 1973), I would like to point out that this theory has to some extent been anticipated by Herodotus (*circa* 485–425 BC) (Book II).

"They proved the truth of most of these assertions, and went on to tell me that the first man to rule Egypt was Min, in whose time the whole country, except the district around Thebes, was marsh, none of the land below Lake Moeris—seven days' voyage up river from the sea—then showing above the water. I have little doubt that they were right in this; for it is clear to any intelligent observer, even if he has no previous information on the subject, that the Egypt to which we sail nowadays is, as it were, the gift of the river and has come only recently into the possession of its inhabitants. The same is true of the country above the lake for the distance of a three days' voyage; the priests said nothing to me about it, but it is precisely the same type of country.

"Now, it is my belief that Egypt itself was originally some such arm of the sea—there were two gulfs, that is, one running from the Mediterranean southwards towards Ethiopia, and the other

northwards from the Indian Ocean towards Syria, and the two almost met at their extreme ends, leaving only a small stretch of country between them. Suppose, now, that the Nile should change its course and flow into this gulf—the Red Sea—what is to prevent it from being silted up by the stream within, say, twenty thousand years? Personally, I think even ten thousand would be enough. That being so, surely in the vast stretch of time which has passed before I was born, a much bigger gulf than this could have been turned into dry land by the silt and brought down by the Nile—for the Nile is a great river and does, in fact, work great changes. So I not only believe the people who gave me this account of Egypt, but my own conclusions strongly support what they said. I have observed for myself that Egypt at the Nile Delta projects into the sea beyond the coast on either side; I have seen shells on the hills and noticed how salt exudes from the soil to such an extent that it affects even the pyramids; I have noticed, too, that the only hill where there is sand is the hill above Memphis, and—a further point—that the soil of Egypt does not resemble that of the neighbouring country of Arabia, or of Libya, or even of Syria (the Mediterranean coast of Arabia is inhabited by Syrians), but is black and friable as one would expect of an alluvial soil formed of the silt brought down by the river from Ethiopia. The soil of Libya is, as we know, reddish and sandy, while in Arabia and Syria it has a larger proportion of stone and clay. I had from the priests another striking piece of evidence about the origin of the country: namely, that in the reign of Moeris the whole area below Memphis used to be flooded when the river rose only twelve feet—and when I got

the information Moeris had been dead for less than nine hundred years.”

Yours faithfully,

D. B. JAMES

*The Doctors' House,
Claremont Road,
Marlow,
Buckinghamshire*

Announcements

Miscellaneous

The following have been elected Foreign Members of the Royal Society.

Professor John Bardeen, **University of Illinois**; Professor Manfred Eigen, **Max-Planck Institute of Physical Chemistry, Göttingen**; Professor Francois Jacob, **Pasteur Institute, Paris**; Professor Ulf Svante Von Euler, **Karolinska Institute, Stockholm**.

The following have been elected Foreign Associates of the National Academy of Sciences, Washington.

Sune Bergstrom, **Karolinska Institutet, Stockholm**; Albert Eschenmoser, **Technische Hochschule, Zurich**; Vladimir A. Engelhardt, **Institute of Molecular Biology, Moscow**; Dennis Gabor, **Imperial College, London**; David V. Glass, **London School of Economics, London**; Jean Goguel, **Ecole des Mines, Paris**; Motto Kimura, **National Institute of Genetics, Japan**; George Klein, **Karolinska Institutet, Stockholm**; Ben Roy Mottelson, **Institute for Theoretical Atomic Physics, Copenhagen**; V. Ramalingaswami, **Institute of Medical Sciences,**

New Delhi; Andrei D. Sakharov, **Lebedev Institute of Physics, Moscow**; I. S. Shklovsky, **Institute of Space Research, Moscow**.

University News

Dr Fredos Papangelou, **University of Göttingen**, has been appointed to the **Chair of Mathematical Statistics** at the **University of Manchester**.

Dr Eric Craig Easson, **University of Glasgow**, has been appointed to the **Chair of Radiotherapy** at the **University of Manchester**.

Dr Peter Joseph Mittler, **Pembroke College, Cambridge**, has been appointed **Professor of the Education of the Mentally Handicapped**, at the **University of Manchester**.

International Meetings

May 25–26, **Stress in Farm Animals**. (Honorary Secretary, Veterinary Field Station, Easterbush, Roslin, Midlothian).

May 30–June 1, **Ducted Propellers**. (Secretary, Royal Institution of Naval Architects, 10 Upper Belgrave Street, London SW1X 8BQ).

June 7–8, **Symposium on The Biology of Hystricomorph Rodents**. (The Assistant Director of Science (UM), The Zoological Society of London, Regent's Park, London NW1 4RY).

June 13–15, **International Conference on Hydrostatic Extrusion**. (Conference Organizer, Birniehill Institute, National Engineering Laboratory, East Kilbride, Glasgow G75 0QU.)

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